HLA-C*06:02 genotype is a predictive biomarker of biologic treatment response in psoriasis

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Abstract

Background: Biologic therapies can be highly effective for the treatment of severe psoriasis but response for individual patients can vary according to drug. Predictive biomarkers to guide treatment selection could improve patient outcomes and treatment cost-effectiveness.

Objective: We sought to test whether *HLA-C*06:02*, the primary genetic susceptibility allele for psoriasis, predisposes patients to respond differently to the two most commonly prescribed biologics for psoriasis, adalimumab (anti-TNF α) and ustekinumab (anti-IL12/23).

Methods: The study utilises a national psoriasis registry that includes longitudinal treatment and response observations and detailed clinical data. HLA alleles were imputed from genome-wide genotype data for 1,326 patients for whom PASI90 response status (90% reduction in psoriasis area and severity index) was observed after 3, 6 or 12 months of treatment. We developed regression models of PASI90 response, examining the interaction between *HLA-C*06:02* and drug type (adalimumab or ustekinumab) while accounting for potentially confounding clinical variables.

Results: HLA-C*06:02 negative patients were significantly more likely to respond to adalimumab than ustekinumab at all time-points (most strongly at 6m: odds ratio (OR) = 2.95, P = 5.85×10⁻⁷) and the difference was greater in HLA-C*06:02 negative patients with psoriatic arthritis (PsA; OR = 5.98, P = 6.89×10⁻⁵). Biologic naive patients that were HLA-C*06:02 positive and PsA negative demonstrated significantly poorer response to adalimumab at 12m (OR = 0.31, P = 3.42×10⁻⁴). Results from HLA-wide analyses were consistent with HLA-C*06:02 itself being the primary effect allele. We found no evidence for genetic interaction between HLA-C*06:02 and ERAP1.

Conclusion: This large observational study suggests that reference to *HLA-C*06:02* status could offer substantial clinical benefit when selecting treatments for severe psoriasis.

Clinical Implications

*HLA-C*06:02* is associated with differential response to adalimumab and ustekinumab in psoriasis patients. Together with psoriatic arthritis status, *HLA-C*06:02* status could inform optimal selection of first-line biologic therapy.

Capsule Summary

In a large observational study, psoriasis patients lacking the susceptibility allele *HLA-C*06:02* demonstrate significantly better response to adalimumab than ustekinumab. The effect is stronger than at other HLA alleles and varies with psoriatic arthritis status.



Key words: psoriasis, psoriatic arthritis, biologic therapy, genetics, pharmacogenetics, treatment response, HLA, adalimumab, ustekinumab, skin disease

Abbreviations used:

BAD British Association of Dermatologists

BADBIR BAD Biologic and Immunomodulators Register

BSTOP Biomarkers of Systemic Treatment Outcomes in Psoriasis

GxE gene-environment interaction

HLA human leukocyte antigen

IL interleukin

MHC major histocompatibility complex

OR odds ratio

PASI psoriasis area and severity index

PsA psoriatic arthritis

TNF tumor necrosis factor

Introduction

Psoriasis is a chronic immune-mediated skin disease with a prevalence of up to 3% in developed nations¹. It is responsible for a high global burden of disability² and the economic impact, in the United States alone, runs into the tens of billions of dollars³. Psoriasis is caused by a complex interplay of genetic and environmental factors not yet fully understood^{4, 5}, and molecular genetic studies have identified more than 60 genomic loci at which variation confers risk of the disease in European populations^{6, 7}.

In recent years the clinical management of psoriasis has been revolutionised by a series of highly effective monoclonal antibody therapies⁸. The most widely adopted of these biologics include adalimumab, which targets TNFα, and ustekinumab, which targets the p40 subunit common to IL-12 and IL-23 and thus inhibits downstream IL-17 signalling. Clinical trials demonstrate that 71% of moderate to severe psoriasis patients achieve a 75% reduction in psoriasis area and severity index (PASI75 response) after 16 weeks of adalimumab treatment, with 45% achieving the superior PASI90 response that is consistent with being "clear" or "nearly clear" of disease⁹. Similarly, ustekinumab induces a PASI75 response within 12 weeks for 67% of patients, and PASI90 response for 39% across dosing groups¹⁰. British Association of Dermatologists (BAD) guidelines recommend that in the absence of relevant contraindications both drugs should be considered equally as first-line biologic therapy for psoriasis, unless active psoriatic arthritis (PsA) is present in which case adalimumab is preferred¹¹. Both drugs are indicated more widely for other immune-mediated inflammatory diseases¹².

Since individuals can respond differently to different biologics, there is great potential to improve patient outcomes and optimise use of these expensive therapies¹³ through the identification of biomarkers that can inform which therapies are most likely to be efficacious. The MHC class I allele *HLA-C*06:02* is a promising candidate biomarker. *HLA-C*06:02* is the genetic variant that makes the largest contribution to psoriasis susceptibility: it accounts for more than 6% of variance in disease risk¹⁴ and each copy of the *HLA-C*06:02* allele carried increases an individual's risk of psoriasis five-fold¹⁵. Its effect is modified by an interaction with genetic variants in the gene *ERAP1*, which encodes a peptide-trimming protein involved in MHC antigen presentation of psoriasis, with *HLA-C*06:02* positive patients experiencing earlier onset, differences in lesion severity and distribution, higher incidence of the Koebner phenomenon and increased likelihood of exacerbation due to streptococcal throat infection¹⁶⁻¹⁸. These differences hint at distinct pathophysiologies and differential response to treatment might therefore be expected. Some evidence has recently accumulated in support of this, with several studies reporting better response

to ustekinumab among *HLA-C*06:02* positive patients than among *HLA-C*06:02* negative patients¹⁹⁻²¹. The relationship between *HLA-C*06:02* and response to anti-TNF agents is unclear²².

With the aim of improving outcomes in individuals with moderate to severe psoriasis we therefore sought to test the hypothesis that *HLA-C*06:02* status is an effective predictive biomarker of response that could be used to inform treatment selection between the two most commonly used biologics, adalimumab and ustekinumab. As such, we have undertaken a retrospective evaluation of *HLA-C*06:02* as a predictive biomarker in a large prospective observational study of biologic interventions in the UK psoriasis population. Our primary definition of positive treatment response is achievement of PASI90, as it correlates with the clinically important status of "clear" or "nearly clear" of psoriasis²³. We consider response at three, six and twelve months after treatment initiation. We consider secondary outcomes of PASI75 and PASI100 response.

Methods

Patient population

The study was conducted in accordance with the 2008 Declaration of Helsinki and in the spirit of the 1996 International Conference on Harmonisation in Good Clinical Practice. Ethical approval for this study was granted by The South East London REC 2 Ethics Committee (11/H0802/7). Written informed consent was obtained from all subjects prior to enrolment.

All participants are adults (>16 years) enrolled in the Biomarkers of Systemic Treatment Outcomes in Psoriasis study (BSTOP; https://www.kcl.ac.uk/lsm/research/divisions/gmm/departments/dermatology/Research/stru/groups/bstop/index.aspx) and the British Association of Dermatologists Biologic and Immunomodulators Register (BADBIR; www.badbir.org). BSTOP is a prospective observational study across 60 UK dermatology centres that includes biological sample collection. It aims to establish clinically relevant markers of outcomes to systemic therapies in severe psoriasis (study protocol: https://www.kcl.ac.uk/ContensisManagedLinks/BSTOP-Protocol-Version-5.pdf). BADBIR is a pharmacovigilance register that has recruited >16,000 psoriasis patients undertaking systemic conventional or biological therapy in the UK and Ireland. It seeks to assess the long-term safety of biologic treatments for psoriasis. Enrolment criteria for the biologic arm for both BSTOP and BADBIR include diagnosis and prescription of systemic therapy by a dermatologist.

Clinical data

Detailed clinical data are recorded by BSTOP and BADBIR at registration and at regular follow-up assessments during the course of routine clinical care. These data include demographics, psoriasis

area and severity index (PASI) assessments of disease severity, treatment details, adverse events and comorbidities. Clinical data were extracted on 1st July 2017. Data derived from BSTOP and BADBIR were merged, and processes were established to identify and resolve inconsistencies between data sources in collaboration with local clinical teams. For a minority of patients appropriate assumptions were employed to demarcate periods of treatment: treatment was considered ongoing where treatment episodes for the same biologic were separated by less than 90 days²⁴; missing treatment end dates were imputed based on the start date of subsequent biologic treatment, allowing a 28 day washout period; and patients were considered to be continuing treatment at the data extract date where no end date was recorded. Age of psoriasis onset was inferred from the recorded year of onset. Patients were assumed to be positive for psoriatic arthritis (PsA) if reported at BADBIR registration or at any subsequent follow-up prior to the data extract date (92.8% diagnosed by a rheumatologist).

Genotype data and HLA imputation

DNA was isolated from blood using standard methods. Genotyping was performed using Illumina HumanOmniExpressExome-8 v1.2 and v1.3 BeadChips followed by quality control using standard tools²⁵⁻²⁸ and procedures as detailed in **Supplementary Methods**. The final dataset was limited to patients of European ancestry. Classical HLA alleles were imputed using SNP2HLA (v1.0.3), based on the T1DGC reference panel²⁹. We excluded poorly imputed alleles ($R^2 < 0.9$) and alleles with frequency <0.01, giving a total of 142 distinct 2- and 4-digit imputed alleles.

Data integration and definition of response

Patients with both genotype data and response data for the first course of treatment for either drug (adalimumab or ustekinumab) were considered for analysis. Patients were required to have a baseline PASI score (up to six months prior to treatment initiation) of >10, and a response PASI score recorded sufficiently close to at least one response time-point (±30 days from 3m; ±60 days from 6m and 12m time-points) while still on treatment. 101 patients with eligible records for both treatments were randomly assigned to the adalimumab or ustekinumab groups (50/51 patients respectively), with their other record being excluded from the analysis. This did not materially impact results (**Table E18**). The final integrated dataset included observations for 1,326 patients.

For each patient observed at each response time-point, PASI90 response was achieved if the response PASI score represented a reduction of 90% or more relative to baseline PASI. Secondary responses of PASI75 and PASI100 were defined similarly.

Statistical modelling

All statistical models were implemented in $R^{27, 30}$. Associations between patient characteristics and drug type were established via regression modelling (linear regression for continuous characteristics; logistic regression for binary characteristics) with drug type (adalimumab vs ustekinumab) as the sole explanatory variable. Associations with HLA-C*06:02 were established using regression models based on imputed HLA-C*06:02 dosage with five ancestry PC covariates based on 108,319 independent SNPs genome-wide^{26, 31, 32}.

At each response time-point, multivariable logistic regression modelling was employed with binary PASI90 response as the dependent variable (PASI75/PASI100 for secondary outcomes) and baseline PASI as a covariate. Drug type and *HLA-C*06:02* dosage were included as main effects and as a drug × *HLA-C*06:02* interaction term: a statistically significant non-zero interaction effect would implicate *HLA-C*06:02* as a predictive biomarker. To generate the full multivariable model accounting for potential clinical confounders, main effect and interaction covariate terms were added based on correlations with *HLA-C*06:02* or drug (**Table 1**). For variables significantly correlated with *HLA-C*06:02* (age of onset, baseline PASI, disease duration and PsA), an interaction term with drug was included, and for variables significantly correlated with drug (PsA and biologic naive status) an interaction term with *HLA-C*06:02* was included. The full model is described in **Supplementary Methods**. Missing observations for age of onset or PsA status covariates were replaced by mean-imputed values derived from *HLA-C*06:02*-positive and negative subgroups. Models of response were fitted within *HLA-C*06:02*- and PsA-defined subgroups; these included a term for drug type and a covariate term for baseline PASI only.

To confirm that our full multivariable model adequately controlled for potential confounding via covariates influencing treatment selection, we repeated the regression analysis with inverse probability of treatment weighting using the propensity score³³. Weighted regression was implemented using the 'survey' package in R³⁴. See **Supplementary Methods** for full details.

HLA-wide analysis was performed for 142 2- and 4-digit alleles having a frequency >1% in our full genotyped cohort of 3,320 patients. The full interaction model was fitted based on imputed dosage for each allele in turn, substituting the HLA-C*06:02 main effect and interaction terms. Conditional analysis was performed by including main effect and interaction terms for both HLA-C*06:02 and the alternative alleles.

ERAP1 interaction analysis was based on the genotyped variant rs27524¹⁵. Psoriasis susceptibility epistasis was confirmed via case-only association testing in the full cohort of 3,320 patients, treating *HLA-C*06:02* status as a binary trait. To test for interaction with respect to adalimumab and ustekinumab response, the full GXE interaction model was supplemented with a

main effect term for rs27524 genotype, first-order interaction terms rs27524 genotype \times *HLA-C*06:02* dosage and rs27524 genotype \times drug, and second-order interaction term rs27524 genotype \times *HLA-C*06:02* dosage \times drug. Power analysis for the *ERAP1* interaction test conducted in the *HLA-C*06:02*-negative subgroup was conducted using the method of Demidenko (https://www.dartmouth.edu/~eugened/power-samplesize.php)³⁵. Assumptions of the method required rs27524 genotype be collapsed to a binary variable (for the purposes of power estimation only); estimates are therefore approximate.

Results

Results section 1: A prospective observational data resource facilitating predictive genetic biomarker identification in psoriasis

To assess the ability of *HLA-C*06:02* to predict different rates of response to adalimumab and ustekinumab we considered 3,320 patients enrolled in the Biomarkers of Systemic Treatment Outcomes in Psoriasis (BSTOP) study and the British Association of Dermatologists Biologic and Immunomodulators Register (BADBIR) for whom genotype data were available (**Methods**). 53.4% of these patients were *HLA-C*06:02* positive (carrying at least one copy of the allele), with 46.6% being *HLA-C*06:02* negative. After applying eligibility criteria to ensure that valid baseline and response PASI scores were available, 1,326 participants were included in the final analyses (**Figure 1**).

Participant baseline characteristics are summarised in **Table 1**. Since our investigation concerns the relationship between HLA-C*06:02 and drug used for treatment (adalimumab or ustekinumab), we sought to identify clinical variables correlated with either of these. We found a strong association between age of psoriasis onset and imputed HLA-C*06:02 dosage (i.e. a probability-weighted estimate of the number of copies of HLA-C*06:02 that a patient carries; $P = 9.38 \times 10^{-22}$), as expected $P = 0.38 \times 10^{-22}$, and the presence of $P = 0.38 \times 10^{-2}$ respectively). The relationship between $P = 0.38 \times 10^{-22}$ and the presence of $P = 0.38 \times 10^{-2}$ but we observed a statistically significant correlation ($P = 0.38 \times 10^{-3}$) that persisted even after controlling for age of psoriasis onset ($P = 0.38 \times 10^{-3}$). $P = 0.38 \times 10^{-3}$ has also significantly associated with drug type ($P = 0.38 \times 10^{-3}$) likely reflecting a tendency towards prescription of anti-TNF therapy for patients with $P = 0.38 \times 10^{-3}$ and methotrexate co-therapy at the start of biologic treatment ($P = 0.38 \times 10^{-3}$). Co-therapy is common in patients with $P = 0.38 \times 10^{-3}$ and indeed the association disappears when controlling for $P = 0.38 \times 10^{-3}$ biologic exposed) was $P = 0.38 \times 10^{-3}$. Finally previous exposure to biologics (biologic naive vs biologic exposed) was

strongly correlated with drug type ($P = 2.12 \times 10^{-32}$), reflecting the frequent use of adalimumab as a first-line biologic in this patient population³⁷; it was not associated with *HLA-C*06:02* genotype (P = 0.411).

The observed rate of PASI90 response to adalimumab (41.9% at 3m; 49.5% at 6m) was consistent with that reported in clinical trials (45% at 16 weeks)⁹, while the observed ustekinumab rate (28.2% at 3m) was lower than the corresponding trial rate (39% at 12 weeks)¹⁰ (**Table 2**). Observed response rates by HLA-C*06:02 status and for PASI75 and PASI100 outcomes are given in **Table E1**.

Results section 2: HLA-C*06:02 is an effective biomarker that could inform treatment selection

We investigated the extent to which *HLA-C*06:02* genotype is predictive of different rates of PASI90 response for adalimumab compared to ustekinumab. Formally, for each time-point (3m, 6m and 12m after treatment initiation) we fitted a logistic regression model for PASI90 response that included an interaction term between imputed *HLA-C*06:02* dosage and drug type (adalimumab and ustekinumab) (**Methods**). These are effectively gene-environment interaction models (GxE), where a statistically significant non-zero interaction term indicates that *HLA-C*06:02* can stratify response.

A significant interaction term was observed in basic models that considered only *HLA-C*06:02* dosage and drug (**Table E2**). However, we took two further steps to ensure that these findings were not primarily driven by the effect of confounding clinical variables reported in **Table 1**. First, we developed multivariable regression models to test for drug × *HLA-C*06:02* interaction that included appropriate main effect and interaction covariate terms (**Methods**). We observed statistically significant non-zero effects at all time-points for the drug × *HLA-C*06:02* interaction term (**Table 2**). The strongest evidence for interaction was observed at the 6m time-point where sample numbers were largest ($P = 3.76 \times 10^{-5}$). A significant interaction effect was also observed for the secondary outcome of PASI75, and for all but the earliest time-point (3m) for PASI100 (**Table E3**).

Second, we employed a propensity-score-weighted approach to adjust for potential confounding via covariates influencing treatment selection (full details in **Supplementary Methods**). We observed that all covariates were well balanced between adalimumab and ustekinumab groups after weighting (**Table E4**, **Figure E1**). The drug × *HLA-C*06:02* interaction terms remained significant at all time-points in the weighted models, at very similar levels of significance to the full unweighted multivariable models (**Table E5**). As such we are confident that our full unweighted model adequately controls for confounding, and all subsequent analyses were based on unweighted models.

To elucidate the observed drug \times *HLA-C*06:02* interaction effect, we examined the effect that drug type exerts on probability of response within two subgroups of patients: *HLA-C*06:02* negative (zero copies of the allele) and *HLA-C*06:02* positive (one or two copies; pooled due to the small number of patients that carry two copies). At all time-points, drug type was associated with PASI90 response among *HLA-C*06:02* negative patients (better response to adalimumab; $OR_{6m} = 2.95$, $P_{6m} = 5.85 \times 10^{-7}$), but not among *HLA-C*06:02* positive patients (**Table 3**, **Figure 2A**). This trend was also observed for the secondary PASI75 and PASI100 outcomes (**Table E6**, **Figure E2**).

We performed separate multivariate regression analyses within adalimumab and ustekinumab groups, including covariate main effects only. These confirmed that while there is some effect size heterogeneity across time-points, HLA-C*06:02 is associated with response to both drugs individually. It is associated with better response to ustekinumab (PASI90 OR_{6m} = 1.72, P_{6m} = 0.018), consistent with previous reports¹⁹⁻²¹, and poorer response to adalimumab (PASI90 OR_{6m} = 0.54, P_{6m} = 1.67×10⁻⁴), which has not previously been established (**Table E7, Figure E3**). The opposite effect directions give rise to the observed drug × HLA-C*06:02 interaction.

Nominally significant interactions are observed between PsA and drug at 12m, and between PsA and HLA-C*06:02 genotype at 3m (**Table 2**). We tested the effect of drug type on PASI90 response within patient subgroups characterised by both HLA-C*06:02 status (positive/negative) and PsA status (presence/absence) (**Table 3**, **Figure 2B**). In HLA-C*06:02 negative patients, the effect of drug type on likelihood of PASI90 response was stronger at all time-points among patients with PsA ($OR_{6m} = 5.98$, $P_{6m} = 6.89 \times 10^{-5}$) than among patients without PsA ($OR_{6m} = 2.32$, $P_{6m} = 1.41 \times 10^{-3}$; not significant at 12m). Conversely, among HLA-C*06:02 positive patients the only significant difference in PASI90 response by drug comprised a weak association in the HLA-C*06:02 positive and PsA negative group at 12m, where adalimumab demonstrated poorer rates of response than ustekinumab (OR = 0.56, P = 0.018). The same trends held true in general for PASI75 and PASI100 outcomes (**Table E8**).

We note that biologic naive status has a stronger direct effect than drug type on the likelihood of achieving PASI90 response (**Table E9**). However, **Table 2** shows clearly that in the full model *HLA-C*06:02* has a significant GxE interaction with drug and not with biologic naive status. The different relative response rates to adalimumab and ustekinumab among *HLA-C*06:02* positive and negative patients are therefore likely to be drug-specific and not explained by these two groups having different propensities to respond to biologic therapy when accounting for previous biologic exposure. Fitting the multivariable GxE models in biologic naive patients only (925 of 1,326 patients) confirmed a drug × *HLA-C*06:02* interaction effect of similar magnitude to the main analysis (**Tables E10 and E11, Figure E4a**). Interestingly, the aforementioned poorer response to adalimumab than

ustekinumab at 12m in HLA-C*06:02 positive and PsA negative patients is much more striking in this biologic naive group ($OR_{12m} = 0.31$, $P_{12m} = 3.42 \times 10^{-4}$) (**Table E11**, **Figure E4b**). When considering biologic experienced patients only the drug \times HLA-C*06:02 interaction effect does not achieve statistical significance at any time-point, potentially due to much smaller sample sizes (**Tables E10** and E11). Nevertheless, the same general trend is observed: the subgroup with the biggest difference in response rates are HLA-C*06:02 negative and PsA positive patients (better response to adalimumab), while HLA-C*06:02 positive and PsA negative patients see marginally better response to ustekinumab (**Figure E5**).

Finally, our data show a trend suggesting that ustekinumab may be more effective than adalimumab at inducing PASI90 response among the subgroup of *HLA-C*06:02* positive patients homozygous for the allele, regardless of PsA status (**Figure E6**). This suggests an additive genetic effect of *HLA-C*06:02* on differential treatment response. Larger sample sizes are required to fully investigate the significance of this observation and its implications for clinical practice.

Results section 3: Among all HLA alleles, HLA-C*06:02 displays the strongest evidence for being a predictive biomarker

While *HLA-C*06:02* has been established as the allele most highly associated with psoriasis susceptibility, it is possible that distinct *HLA-C* alleles or alleles of other class I or class II MHC genes might elicit an enhanced anti-drug immune response to one of the drugs and consequently better predict differential treatment response. We therefore repeated our analysis for all 142 2- and 4-digit HLA alleles that were imputed with high confidence (**Methods**), using the same full GxE model as for *HLA-C*06:02* (**Table E12**). We confirmed that *HLA-C*06:02* displays the strongest evidence for a drug × HLA allele interaction for 6m PASI90 response, demonstrating statistical significance at a Bonferroni-corrected p-value threshold of 1.17×10⁻⁴ (based on 426 tests: 142 alleles × 3 time-points) (**Figure 3**). Results at other time-points were not inconsistent with this, no HLA alleles achieving significance at the Bonferroni-corrected threshold (**Table E12**). A similar pattern was also observed for the secondary PASI75 and PASI100 outcomes (**Table E12**, **Figure E7**). These findings suggest that *HLA-C*06:02* is likely to be the primary effect allele contributing to biologic response, but due to the extensive linkage disequilibrium across this region larger samples will be necessary to fully investigate the role of other HLA alleles.

To identify potential independent secondary predictive biomarkers in the HLA region, we also report the most associated 2- and 4-digit HLA alleles after conditioning on HLA-C*06:02 (main and interaction terms) (**Table E13**). No alleles achieved p-values below the Bonferroni-corrected significance threshold of 1.17×10^{-4} . The smallest p-values were observed for other HLA-C alleles and

for *HLA-B* alleles; we found little evidence to support independent secondary predictive biomarkers at MHC class II genes. Note that full results for all HLA alleles are provided in **Table E14**.

Results section 4: No evidence observed for an interaction with ERAP1 genotype

Variants such as rs27524 in *ERAP1* exhibit an epistatic effect on psoriasis susceptibility through interaction with HLA-C*06:02, with each copy of the risk allele amplifying the increase in disease risk that positive HLA-C*06:02 status confers¹⁵. Case-only analysis in our full cohort of 3,320 patients supports this interaction: rs27524 is strongly associated with HLA-C*06:02 status (OR = 1.35, P = 5.91×10⁻⁹).

We sought to establish whether a similar effect is observed for differential response to adalimumab versus ustekinumab. We found no evidence for epistasis based on two complementary approaches: a full model including the second-order interaction term rs27524 genotype × *HLA-C*06:02* dosage × drug (effectively a gene-gene-environment (GxGxE) model; **Table E15**), and a simple GxE model within the subgroup of 622 *HLA-C*06:02* negative patients (in which differential response by drug was previously observed) that included the interaction term rs27524 genotype × drug (**Table E16**). When removing the (non-significant) second-order interaction term from the GxGxE model, significant p-values are observed for *HLA-C*06:02* dosage × drug, as expected, but for neither interaction term involving the *ERAP1* variant (**Table E17**).

We estimate that our sample sizes provide 80% power to detect interactions between *ERAP1* and drug in the *HLA-C*06:02* negative subgroup when interaction effect sizes (beta regression parameters) are larger than 1.62, 1.28 and 1.37 at 3m, 6m and 12m respectively. Since such effects were not observed we find no evidence to suggest that an interaction between *ERAP1* and *HLA-C*06:02* could provide a more effective predictive biomarker than *HLA-C*06:02* alone. A similar conclusion holds when considering the secondary outcomes, PASI75 and PASI100 (**Tables E15, E16 and E17**).

Discussion

This study constitutes the largest investigation to date into the pharmacogenetics of biologic response in psoriasis, and the first to utilise jointly generated clinical and genetic data on different drugs to identify a predictive biomarker with potential clinical utility. We report that the *HLA-C*06:02* allele effectively stratifies psoriasis patients into groups with different profiles of response to the two most frequently prescribed biologics, adalimumab and ustekinumab.

While the scale of our clinical data resource makes it highly representative of the UK psoriasis population^{38, 39}, limitations include the heterogeneous nature of the response data, which

lack a structured series of PASI observations at fixed time-points. This limits more formal longitudinal analyses. Similarly, baseline PASI scores are defined pragmatically. They can precede treatment by up to six months and may have been recorded during alternative treatment, although we took steps to minimise any resulting bias (**Methods**). Adverse drug reactions, not investigated here, represent another important consideration when selecting treatment. Independent replication will be important, although our findings concord with previous studies that consider adalimumab and ustekinumab separately¹⁹⁻²².

Our results demonstrate that *HLA-C*06:02* negative psoriasis patients are significantly more likely to respond to adalimumab than to ustekinumab, but that there is no significant benefit to adalimumab over ustekinumab in *HLA-C*06:02* positive patients.

We also find that the effect of *HLA-C*06:02* is modulated by the presence or absence of comorbid PsA, with adalimumab conferring the greatest benefit over ustekinumab in patients that are *HLA-C*06:02* negative and PsA positive (31.9% of all patients with PsA status available). Interestingly, these findings demonstrate the effectiveness of adalimumab at treating psoriatic skin disease only. Further investigation of the ability of HLA genes to predict combined skin and joint response for PsA positive psoriasis patients is therefore warranted – ideally via longitudinal studies that collect separate validated objective measurements for both skin and joint involvement.

Through HLA imputation we estimated that 46.6% of severe psoriasis patients are HLA-C*06:02 negative. While treatment selection should always be considered on a case-by-case basis¹¹, our results suggest that a default strategy of ascertaining HLA-C*06:02 status and administering adalimumab as first-line biologic to HLA-C*06:02 negative patients may be an effective approach. Of the 53.4% of patients that are HLA-C*06:02 positive, Table 1 suggests that more than three-quarters will not have active PsA. This group may benefit from ustekinumab as a default firstline treatment over the longer term (Figure E4), particularly in light of its longer dosing intervals and better persistence relative to adalimumab 40. Our findings are not conclusive for patients that are HLA-C*06:02 positive and PsA positive. Since adalimumab is already the recommended first-line biologic in the UK when PsA is present¹¹, our recommendations primarily impact the 71.8% of patients without active PsA (Table 1). HLA-C*06:02-informed treatment selection could therefore offer improved likelihood of PASI90 response through the first 12 months of treatment for 35.9% of all severe psoriasis patients, compared to random assignment to adalimumab or ustekinumab. We acknowledge that random assignment does not reflect current clinical practice in this patient population³⁷. However, current UK guidelines do not favour either adalimumab or ustekinumab in the absence of PsA¹¹, and prescribing practices evolve over time and vary by region. We also note

that our recommendations will have health economic implications as adalimumab biosimilars emerge.

The results presented here support the notion that *HLA-C*06:02* positive and *HLA-C*06:02* negative plaque psoriasis represent biologically distinct pathologies, or endotypes. Differences in presentation have long been recognised¹⁶. However, we suggest that with the implications for clinical decision-making raised by our findings, *HLA-C*06:02* status represents a more relevant stratification of psoriasis patients than the primarily age-of-onset delimited type I/type II distinction⁴¹.

It is widely accepted that HLA-C*06:02 is the genetic allele that makes by far the largest individual contribution to the risk of developing psoriasis⁴²⁻⁴⁴. Intriguingly, our HLA-wide analysis suggests that this allele is also mechanistically relevant to biologic response among patients (**Figure 3**, **Table E12**). As such, it is unlikely that HLA-C*06:02 should generalise as a predictive biomarker for biologic response in other immune-mediated inflammatory diseases. Conversely, these findings may shed important light on the complex pathogenic mechanisms underlying psoriasis. The difference in response to the two drugs among HLA-C*06:02 negative patients suggests that aberrant signalling of immune pathways downstream of TNF α , adalimumab's target molecule, may play a more prominent role in the development and maintenance of psoriatic lesions for these individuals than for HLA-C*06:02 positive patients.

Further investigation of the genetic, transcriptomic and immunological differences between *HLA-C*06:02* positive and negative patients could offer vital insights into the pathophysiology of psoriasis and mechanisms of treatment response. Much larger sample sizes will be required to provide sufficient statistical power to accurately quantify the effect of *HLA-C*06:02* and refine the contributions of other HLA alleles. More generally, genome-wide analyses have the potential to uncover genetic contributions to treatment response beyond the HLA region. The genotype data utilised in this study will contribute to such efforts, and results are eagerly anticipated. With respect to clinical application, the potential impact of our findings on patient outcomes is substantial, but it will be important to validate our findings more formally in an appropriately structured prospective clinical trial setting. The design of such a trial should also formally account for PsA status and the clinical factors most likely to confound observational studies, such as previous biologic exposure.

In summary, we show that *HLA-C*06:02* status is a predictive biomarker that influences response to adalimumab and ustekinumab. Ascertainment of *HLA-C*06:02* genotype is straightforward, and our results could have substantial clinical relevance when selecting between two of the most commonly used biologic treatments for psoriasis.

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Table 1 –Summary statistics for baseline characteristics and potential confounding clinical variables

Negative *HLA-C*06:02* status: no copies of the allele; positive status: one or two copies of the allele; PASI: Psoriasis Area and Severity Index. P-values indicated are derived from regression modelling (linear/logistic regression for continuous/binary characteristics respectively); in particular, the *HLA-C*06:02* p-values are based on imputed *HLA-C*06:02* dosage after controlling for five ancestry principal components.

	All motionts		By drug		By HLA-C*06:02 status			
	All patients	Adalimumab	Ustekinumab) P	Negative	Positive	Р	
N	1,326	839	487		622	704		
Baseline PASI score (mean ± SD)	16.7 ± 6.4	16.8 ± 6.5	16.6 ± 6.3	0.551	17.1 ± 6.6	16.4 ± 6.3	0.031	
Age of disease onset (mean ± SD) ^a	21.8 ± 12.6	21.4 ± 12.2	22.4 ± 13.2	0.173	25.6 ± 12.8	18.5 ± 11.4	9.38×10 ⁻²²	
Disease duration at treatment start (years; mean ± SD) ^a	23.3 ± 12.6	22.8 ± 12.1	24.0 ± 13.4	0.121	20.7 ± 11.5	25.5 ± 13.1	3.61×10 ⁻⁹	
Psoriatic arthritis (%) ^b	28.2	30.5	24.2	0.017	32.3	24.6	8.44×10 ^{-3 c}	
Biologic naïve (%)	69.8	81.5	49.5	2.12×10 ⁻³²	69.3	70.2	0.411	
Methotrexate co-therapy at treatment start (%)	11.3	12.4	9.4	0.103	13.7	9.2	0.027 ^d	

^a Based on 1,177 patients (89%) with age of disease onset recorded; ^b Based on 1,275 patients (96%) with PsA status recorded; ^c P = 3.98×10^{-3} when controlling for age of onset; ^d P = 0.097 when controlling for presence of PsA

Table 2 – HLA-C*06:02 is a predictive biomarker of PASI90 response to adalimumab or ustekinumab after accounting for potential confounding variables

Results are presented for the model interaction terms only. Results for other model terms are not shown; in particular main effect terms are not unambiguously interpretable in the presence of an interaction term. **Table 3** further elucidates the effects of *HLA-C*06:02* and PsA status.

	PASI90 response				
	3 months	6 months	12 months		
n adalimumab	401	586	514		
adalimumab responders	168 (41.9%)	290 (49.5%)	257 (50.0%)		
n ustekinumab	245	325	298		
ustekinumab responders	69 (28.2%)	130 (40.0%)	139 (46.6%)		
n total	646	911	812		
Drug × BL PASI interaction					
Effect size (beta)	-0.045	0.038	-0.010		
95% CI	(-0.109, 0.018)	(-0.008, 0.084)	(-0.062, 0.043)		
P-value	0.162	0.162 0.108			
Drug × Age of Onset interaction					
Effect size (beta)	0.009	-0.003	-0.001		
95% CI	(-0.026, 0.044)	(-0.031, 0.026)	(-0.030, 0.028)		
P-value	0.605	0.861	0.932		
Drug × Disease Duration interaction					
Effect size (beta)	0.024	-0.014	0.001		
95% CI	(-0.009, 0.058)	(-0.043, 0.014)	(-0.028, 0.031)		
P-value	0.156	0.329	0.928		
Drug × PsA interaction					
Effect size (beta)	-0.102	0.491	0.934		
95% CI	(-1.000, 0.795)	(-0.209, 1.191)	(0.215, 1.654)		
P-value	0.823	0.169	0.011		
HLA-C*06:02 × PsA interaction					
Effect size (beta)	-0.926	-0.175	0.327		
95% CI	(-1.649, -0.203)	(-0.725, 0.374)	(-0.261, 0.916)		
P-value	0.012	0.531	0.276		
HLA-C*06:02 × Biologic Naive interaction					
Effect size (beta)	-0.326	0.101	0.152		
95% CI	(-1.079, 0.427)	(-0.495, 0.696)	(-0.464, 0.768)		
P-value	0.396	0.741	0.629		
Drug × HLA-C*06:02 interaction					
Effect size (beta)	-0.901	-1.198	-0.921		
95% CI	(-1.641, -0.161)	(-1.768, -0.628)	(-1.503, -0.340)		
P-value	0.017	3.76×10 ⁻⁵	1.90×10 ⁻³		

Table 3 – Association of drug type with PASI90 response by *HLA-C*06:02* status and presence of concomitant psoriatic arthritis

PsA: psoriatic arthritis (concomitant with psoriasis – see **Methods** for PsA definition; note that PsA subgroup numbers sum to less than "All" numbers, due to a minority of patients without PsA status recorded).

	All			Subgroup without PsA			Subgroup with PsA		
	3 months	6 months	12 months	3 months	6 months	12 months	3 months	6 months	12 months
HLA-C*06:02 Negative						Y			
n adalimumab	195	265	243	124	159	160	66	100	79
adalimumab responders	80 (41.0%)	154 (58.1%)	133 (54.7%)	47 (37.9%)	87 (54.7%)	86 (53.8%)	33 (50.0%)	62 (62.0%)	44 (55.7%)
n ustekinumab	113	153	137	83	109	93	26	38	39
ustekinumab responders	20 (17.7%)	50 (32.7%)	55 (40.1%)	16 (19.3%)	39 (35.8%)	43 (46.2%)	3 (11.5%)	8 (21.1%)	9 (23.1%)
n total	308	418	380	207	268	253	92	138	118
Drug: adalimumab vs ustekinumab									
Odds ratio	3.271	2.950	1.860	2.586	2.316	1.430	7.423	5.977	4.076
95% CI	(1.846, 5.795)	(1.930, 4.510)	(1.207, 2.867)	(1.330, 5.027)	(1.383, 3.878)	(0.845, 2.420)	(1.984, 27.769)	(2.478, 14.417)	(1.707, 9.733)
P-value	4.91×10 ⁻⁵	5.85×10 ⁻⁷	4.94×10 ⁻³	5.10×10 ⁻³	1.41×10 ⁻³	0.182	2.90×10 ⁻³	6.89×10 ⁻⁵	1.55×10 ⁻³
HLA-C*06:02 Positive									
n adalimumab	206	321	271	150	231	198	47	82	65
adalimumab responders	88 (42.7%)	136 (42.4%)	124 (45.8%)	69 (46.0%)	99 (42.9%)	84 (42.4%)	17 (36.2%)	33 (40.2%)	36 (55.4%)
n ustekinumab	132	172	161	91	128	115	35	37	41
ustekinumab responders	49 (37.1%)	80 (46.5%)	84 (52.2%)	35 (38.5%)	60 (46.9%)	63 (54.8%)	12 (34.3%)	15 (40.5%)	19 (46.3%)
n total	338	493	432	241	359	313	82	119	106
Drug: adalimumab vs									
ustekinumab									
Odds ratio	1.266	0.841	0.738	1.366	0.846	0.565	1.057	0.978	1.461
95% CI	(0.806, 1.987)	(0.579, 1.221)	(0.495, 1.102)	(0.801, 2.329)	(0.548, 1.307)	(0.351, 0.907)	(0.417, 2.680)	(0.442, 2.166)	(0.657, 3.251)
P-value	0.306	0.362	0.137	0.252	0.451	0.018	0.907	0.957	0.353

Figure Legends

Figure 1 – Flow diagram of study eligibility

BADBIR: British Association of Dermatologists Biologic and Immunomodulators Register; BSTOP: Biomarkers of Systemic Treatment Outcomes in Psoriasis; PASI: Psoriasis Area and Severity Index.

Figure 2 – Differential effect of adalimumab and ustekinumab depends on *HLA-C*06:02* status and can be further discriminated by presence of concomitant psoriatic arthritis

Proportion of patients achieving PASI90 response: (**A**) by *HLA-C*06:02* status (negative: no copies of the allele; positive: one or two copies of the allele); (**B**) by *HLA-C*06:02* status and PsA status. Displayed 95% confidence intervals are derived from the Bayesian credible interval using the Jeffreys prior. PsA: psoriatic arthritis (concomitant with psoriasis – see **Methods** for PsA definition).

Figure 3 – GxE interaction p-values for PASI90 response across common 2- and 4-digit HLA alleles Top panel: GxE interaction p-value by HLA allele; bottom panel: GxE interaction p-value by HLA allele after conditioning on *HLA-C*06:02* main effect and interaction terms; y-axis: -log₁₀(p-value); dark red dashed line: Bonferroni-corrected significance threshold of 1.17×10⁻⁴; grey dashed line: nominal significance threshold of 0.05. Time-points are represented by different shaped points. Note that the x-axis represents HLA allele as a categorical variable ordered lexicographically, and does not represent scaled chromosome position. In each panel the most significantly associated allele at each time-point is labelled and highlighted by a grey circle. For ease of identification *HLA-C*06:02* p-values for the three time-points are joined by a dotted green line; there are no *HLA-C*06:02* p-values for the conditional tests.

BADBIR/BSTOP patients with genotype data **3,320**

Exposed to biologic therapy **2,596**

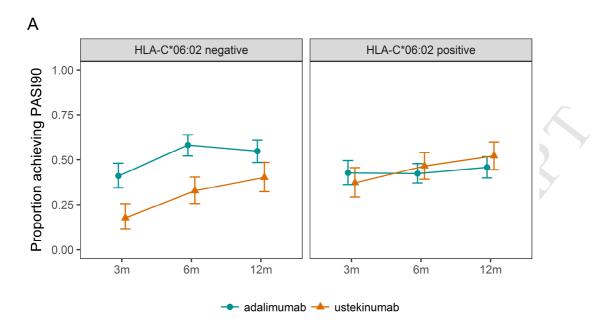
Exposed to adalimumab or ustekinumab **2,319**

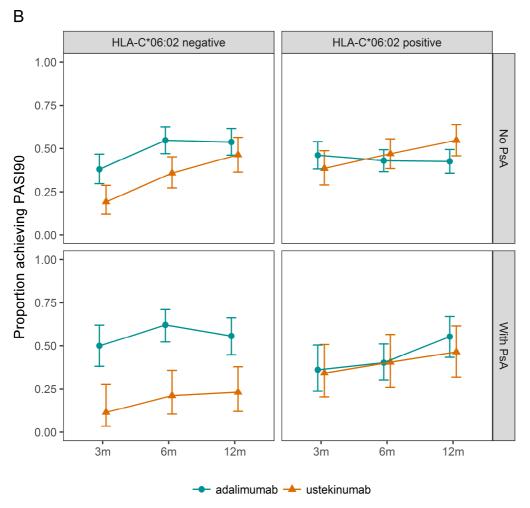
Response data (PASI score) available for first course of adalimumab or ustekinumab

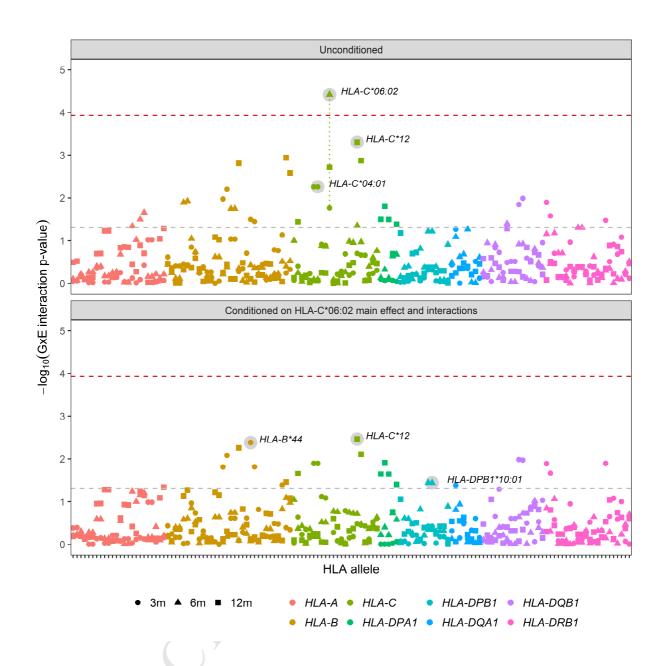
1,981

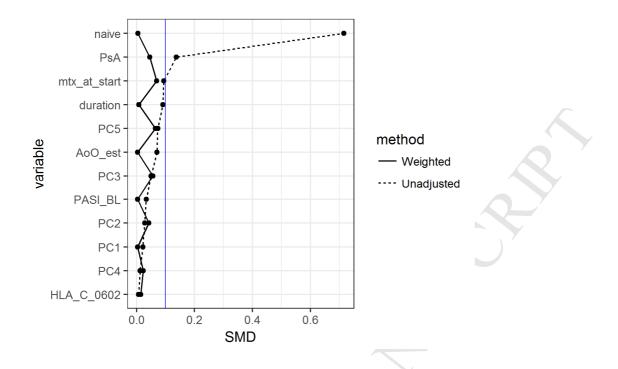
Baseline PASI score available and > 10
1,326

Response Response Response data at 3m data at 6m data at 12m 812

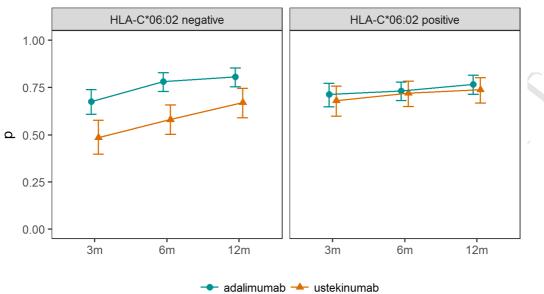




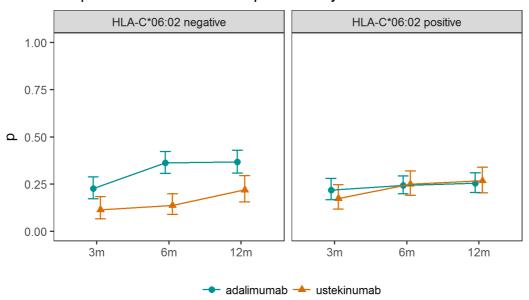




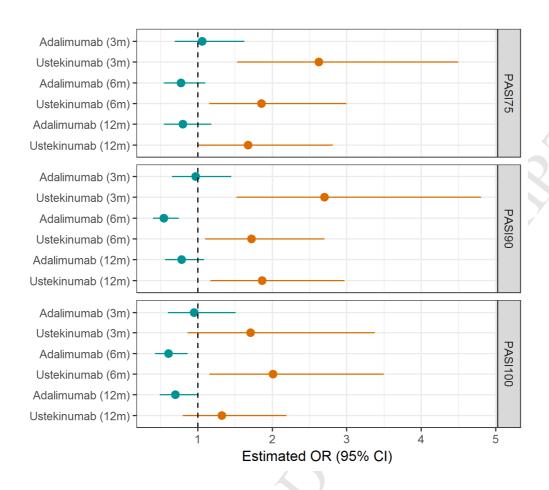
Proportion of PASI75 responders by HLA-C*06:02 status

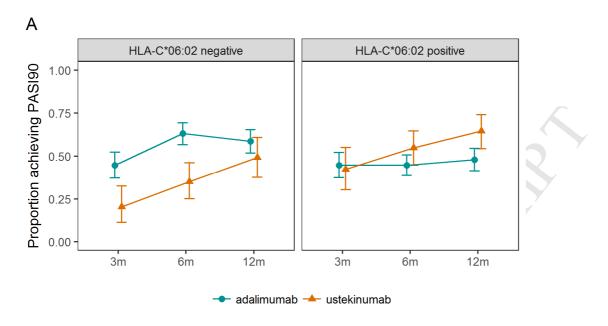


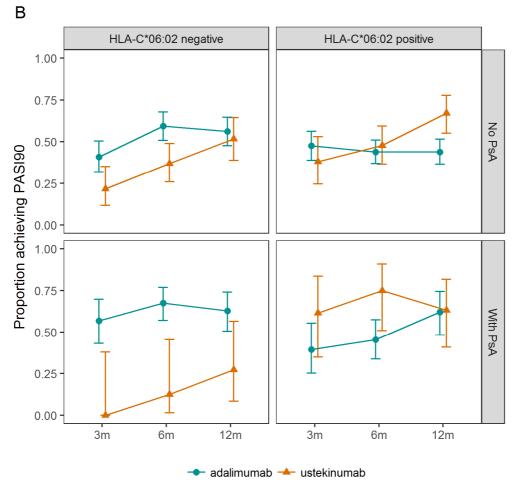
Proportion of PASI100 responders by HLA-C*06:02 status

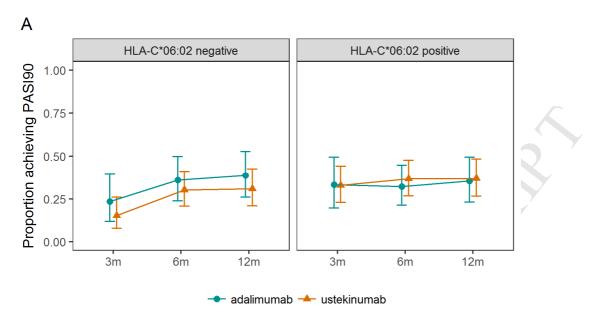


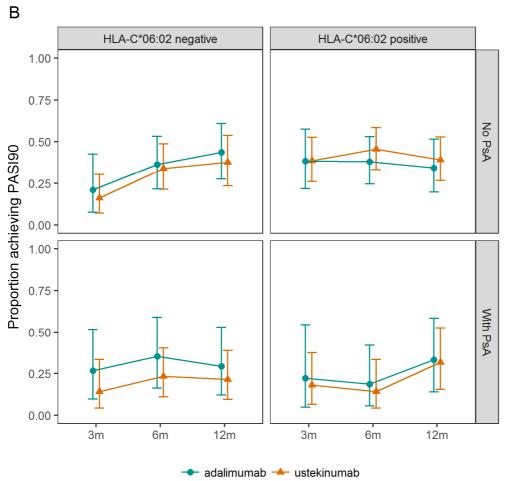


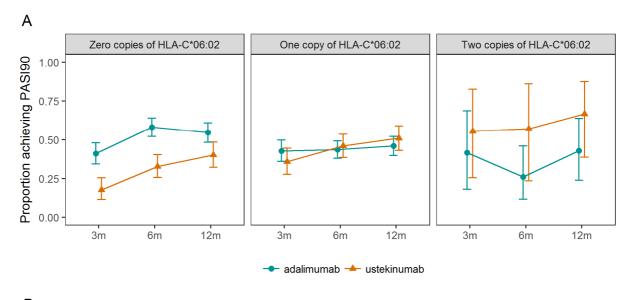


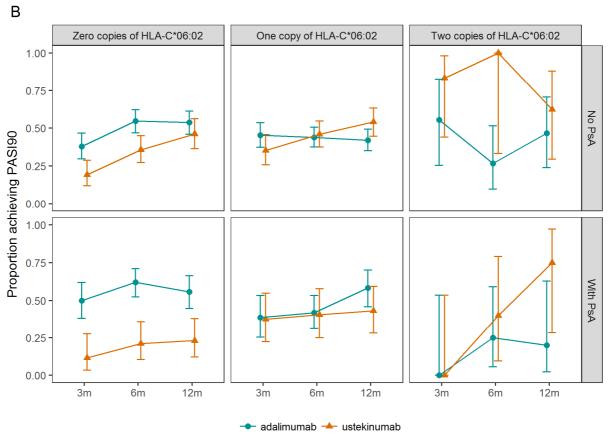


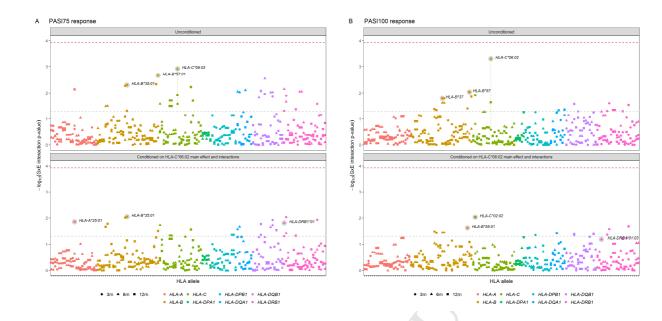












Online Repository Materials

*HLA-C*06:02* genotype is a predictive biomarker of biologic treatment response in psoriasis vulgaris

Nick Dand, Michael Duckworth, David Baudry, Alice Russell, Charles J. Curtis, Sang Hyuck Lee, Ian Evans, Kayleigh J. Mason, Ali Alsharqi, Gabrielle Becher, A. David Burden, Richard G. Goodwin, Kevin McKenna, Ruth Murphy, Gayathri K. Perera, Radu Rotarescu, Shyamal Wahie, Andrew Wright, Nick J. Reynolds, Richard B. Warren, Christopher E. M. Griffiths, Catherine H. Smith*, Michael A. Simpson*, and Jonathan N. Barker*, on behalf of the BADBIR study group, the BSTOP study group and the PSORT consortium

Figure E1 – Standardised mean differences in covariates between adalimumab and ustekinumab treatment groups before and after inverse probability of treatment weighting using the propensity score

Figure E2 – Differential effect of adalimumab and ustekinumab depends on HLA-C*06:02 status

Figure E3 – Size of HLA-C*06:02 main effect on PASI75, PASI90 and PASI100 response by drug

Figure E4 – Differential effect of adalimumab and ustekinumab by *HLA-C*06:02* status and psoriatic arthritis status, in biologic naive patients only

Figure E5 – Differential effect of adalimumab and ustekinumab by *HLA-C*06:02* status and psoriatic arthritis status, in biologic experienced patients only

Figure E6 – Cohort analysis suggests that the differential effect of adalimumab and ustekinumab by *HLA-C*06:02* status and psoriatic arthritis status extends to genotype

Figure E7 - GxE interaction p-values for PASI75 and PASI100 response across common 2- and 4-digit HLA alleles

Table E1 – Observed PASI75, PASI90 and PASI100 response rates by drug and HLA-C*06:02 status

Table E2 – Significant interaction of drug and *HLA-C*06:02* genotype in achievement of PASI90 response (uncorrected model)

Table E3 – Significant interaction of drug and *HLA-C*06:02* status in achievement of PASI75 and PASI100 response when accounting for potential confounding variables

- **Table E4** Distribution of covariates between adalimumab and ustekinumab treatment groups before and after inverse probability of treatment weighting using the propensity score
- **Table E5** Significant interaction of drug and *HLA-C*06:02* status in achievement of PASI75, PASI90 and PASI100 response based on inverse probability of treatment weighting using the propensity score
- Table E6 Association of drug type with PASI75 and PASI100 response by HLA-C*06:02 status
- **Table E7** *HLA-C*06:02* genotype associates with response to either drug
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- Table E12 HLA alleles with strongest evidence for interaction with drug
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- Table E14 Full drug × HLA allele interaction test results for all HLA alleles
- Table E15 GxGxE test results for interaction between HLA-C*06:02 and ERAP1 variant rs27524
- **Table E16** GxE model for drug and *ERAP1* genotype among patients that are *HLA-C*06:02* negative
- Table E17 Test results for HLA-C*06:02 and ERAP1 model excluding GxGxE term
- Table E18 GxE test results for which duplicated patients are excluded from both groups

Supplementary Methods

Figure E1 – Standardised mean differences in covariates between adalimumab and ustekinumab treatment groups before and after inverse probability of treatment weighting using the propensity score

Covariates ordered by size of SMD before inverse probability of treatment weighting adjustment. Blue line indicates accepted threshold of 0.1 below which covariates are effectively balanced between treatment groups. SMD: standardised mean difference; PsA: psoriatic arthritis; mtx: methotrexate; PC: (ancestry) principal component; AoO_est: estimated age of disease onset (including imputed values; see **Methods**); PASI_BL: baseline PASI.

Figure E2 - Differential effect of adalimumab and ustekinumab depends on *HLA-C*06:02* **status** Proportion of patients achieving PASI75 or PASI100 response, by *HLA-C*06:02* status (negative: no copies of the allele; positive: one or two copies of the allele). Displayed 95% confidence intervals are derived from the Bayesian credible interval using the Jeffreys prior.

Figure E3 – Size of *HLA-C*06:02* main effect on PASI75, PASI90 and PASI100 response by drug OR: odds ratio; CI: confidence interval.

Figure E4 - Differential effect of adalimumab and ustekinumab by *HLA-C*06:02* status and psoriatic arthritis status, in biologic naive patients only

Proportion of biologic naive patients achieving PASI90 response: (**A**) by *HLA-C*06:02* status (negative: no copies of the allele; positive: one or two copies of the allele); (**B**) by *HLA-C*06:02* status and PsA status. Displayed 95% confidence intervals are derived from the Bayesian credible interval using the Jeffreys prior. PsA: psoriatic arthritis (concomitant with psoriasis – see Methods for PsA definition).

Figure E5 - Differential effect of adalimumab and ustekinumab by *HLA-C*06:02* status and psoriatic arthritis status, in biologic experienced patients only

Proportion of biologic experienced patients achieving PASI90 response: (**A**) by *HLA-C*06:02* status (negative: no copies of the allele; positive: one or two copies of the allele); (**B**) by *HLA-C*06:02* status and PsA status. Displayed 95% confidence intervals are derived from the Bayesian credible interval using the Jeffreys prior. PsA: psoriatic arthritis (concomitant with psoriasis – see Methods for PsA definition).

Figure E6 – Cohort analysis suggests that the differential effect of adalimumab and ustekinumab by *HLA-C*06:02* status and psoriatic arthritis status extends to genotype

Proportion of patients achieving PASI90 response: (**A**) by *HLA-C*06:02* genotype; (**B**) by *HLA-C*06:02* genotype and PsA status. Displayed 95% confidence intervals are derived from the Bayesian credible interval using the Jeffreys prior. PsA: psoriatic arthritis (concomitant with psoriasis – see **Methods** for PsA definition).

Figure E7 - GxE interaction p-values for PASI75 and PASI100 response across common 2- and 4-digit HLA alleles

(a) PASI75 response; (b) PASI100 response. Top panel: GxE interaction p-value by HLA allele; bottom panel: GxE interaction p-value by HLA allele after conditioning on *HLA-C*06:02* main effect and interaction terms; y-axis: -log10(p-value); dark red dashed line: Bonferroni-corrected significance threshold of 1.17×10⁻⁴; grey dashed line: nominal significance threshold of 0.05. Time-points are represented by different shaped points. Note that the x-axis represents HLA allele as a categorical variable ordered lexicographically, and does not represent scaled chromosome position. In each panel the most significantly associated allele at each time-point is labelled and highlighted by a grey circle. For ease of identification *HLA-C*06:02* p-values for the three time-points are joined by a dotted green line; there are no *HLA-C*06:02* p-values for the conditional tests.

Table E1 – Observed PASI75, PASI90 and PASI100 response rates by drug and *HLA-C*06:02* status

		Adalimumab			Ustekinumab	
	<i>HLA-C*06:02</i> Positive	HLA-C*06:02 Negative	Total	HLA-C*06:02 Positive	HLA-C*06:02 Negative	Total
3m time-point						
n	206	195	401	132	113	245
PASI75 response	147 (71.4%)	132 (67.7%)	279 (69.6%)	90 (68.2%)	55 (48.7%)	145 (59.2%)
PASI90 response	88 (42.7%)	80 (41.0%)	168 (41.9%)	49 (37.1%)	20 (17.7%)	69 (28.2%)
PASI100 response	45 (21.8%)	44 (22.6%)	89 (22.2%)	23 (17.4%)	13 (11.5%)	36 (14.7%)
6m time-point						
n	321	265	586	172	153	325
PASI75 response	235 (73.2%)	207 (78.1%)	442 (75.4%)	124 (72.1%)	89 (58.2%)	213 (65.5%)
PASI90 response	136 (42.4%)	154 (58.1%)	290 (49.5%)	80 (46.5%)	50 (32.7%)	130 (40.0%)
PASI100 response	78 (24.3%)	96 (36.2%)	174 (29.7%)	43 (25.0%)	21 (13.7%)	64 (19.7%)
12m time-point						
n	271	243	514	161	137	298
PASI75 response	208 (76.8%)	196 (80.7%)	404 (78.6%)	119 (73.9%)	92 (67.2%)	211 (70.8%)
PASI90 response	124 (45.8%)	133 (54.7%)	257 (50.0%)	84 (52.2%)	55 (40.1%)	139 (46.6%)
PASI100 response	69 (25.5%)	89 (36.6%)	158 (30.7%)	43 (26.7%)	30 (21.9%)	73 (24.5%)

Table E2 – Significant interaction of drug and *HLA-C*06:02* genotype in achievement of PASI90 response (uncorrected model)

Based on logistic regression model of PASI90 response that includes baseline PASI and five ancestry principal components as the only covariates (no adjustment for clinical confounders). Results are presented only for the drug \times *HLA-C*06:02* interaction term in the GxE model. Results for other model terms are not shown; in particular the terms for *HLA-C*06:02* and drug main effects are not unambiguously interpretable (due to the presence of an interaction term between the two, the value of each main effect term depends on the precise coding of the other).

		PASI90 response	
	3 months	6 months	12 months
n adalimumab	401	586	514
n ustekinumab	245	325	298
n total	646	911	812
Drug × HLA-C*06:02 interaction			
Effect size (beta)	-0.894	-1.221	-0.859
95% CI	(-1.535, -0.253)	(-1.739, -0.702)	(-1.382, -0.337)
P-value	6.25×10 ⁻³	3.94×10 ⁻⁶	1.27×10 ⁻³

Table E3 – Significant interaction of drug and *HLA-C*06:02* status in achievement of PASI75 and PASI100 response when accounting for potential confounding variables

		PASI75 response		Q	PASI100 response	
	3 months	6 months	12 months	3 months	6 months	12 months
n adalimumab	401	586	514	401	586	514
n ustekinumab	245	325	298	245	325	298
n total	646	911	812	646	911	812
Drug × BL PASI interaction			1			
Effect size (beta)	-0.032	0.033	-0.061	-0.021	0.051	0.025
95% CI	(-0.101, 0.037)	(-0.018, 0.084)	(-0.125, 0.004)	(-0.095, 0.053)	(-0.003, 0.105)	(-0.029, 0.079)
P-value	0.365	0.208	0.065	0.583	0.063	0.364
Drug × Age of Onset interaction			KV.			
Effect size (beta)	0.008	-0.001	-0.003	0.019	0.012	-0.015
95% CI	(-0.026, 0.043)	(-0.032, 0.031)	(-0.038, 0.033)	(-0.024, 0.062)	(-0.022, 0.046)	(-0.046, 0.016)
P-value	0.634	0.969	0.886	0.390	0.488	0.351
Drug × Disease Duration interaction		$\langle \rangle$				
Effect size (beta)	0.028	-0.003	-0.008	0.030	0.011	-0.007
95% CI	(-0.006, 0.061)	(-0.034, 0.028)	(-0.041, 0.025)	(-0.010, 0.071)	(-0.023, 0.046)	(-0.040, 0.025)
P-value	0.105	0.851	0.639	0.143	0.519	0.662
Drug × PsA interaction	^					
Effect size (beta)	-0.443	0.836	0.924	-0.725	0.234	0.854
95% CI	(-1.267, 0.381)	(0.114, 1.557)	(0.139, 1.709)	(-1.777, 0.327)	(-0.611, 1.079)	(0.042, 1.666)
P-value	0.292	0.023	0.021	0.177	0.587	0.039
HLA-C*06:02 × PsA interaction						
Effect size (beta)	-0.782	0.022	0.248	-0.743	-0.262	0.107
95% CI	(-1.488, -0.077)	(-0.566, 0.611)	(-0.424, 0.920)	(-1.588, 0.103)	(-0.885, 0.362)	(-0.530, 0.744)
P-value	0.030	0.941	0.470	0.085	0.411	0.743

HLA-C*06:02 × Biologic Naive interaction						
Effect size (beta)	-0.184	0.387	0.412	-0.372	-0.048	-0.029
95% CI	(-0.909, 0.541)	(-0.229, 1.003)	(-0.260, 1.083)	(-1.264, 0.519)	(-0.788, 0.692)	(-0.718, 0.661)
P-value	0.619	0.218	0.230	0.413	0.899	0.935
Drug × HLA-C*06:02 interaction						
Effect size (beta)	-0.832	-1.026	-0.854	-0.504	-1.199	-0.724
95% CI	(-1.568, -0.097)	(-1.648, -0.405)	(-1.521, -0.187)	(-1.377, 0.369)	(-1.874, -0.524)	(-1.349, -0.100)
P-value	0.026	1.21×10 ⁻³	0.012	0.258	5.00×10 ⁻⁴	0.023

Table E4 – Distribution of covariates between adalimumab and ustekinumab treatment groups before and after inverse probability of treatment weighting using the propensity score

SMD: standardised mean difference.

		Pre-weighting			Post-weighting	
	Adalimumab (mean (sd))	Ustekinumab (mean (sd))	SMD	Adalimumab (mean (sd))	Ustekinumab (mean (sd))	SMD
n	487	839		1309.66	1332.66	
Baseline PASI	16.60 (6.27)	16.81 (6.50)	0.034	16.62 (6.33)	16.65 (6.36)	0.004
Biologic naive	0.49 (0.50)	0.82 (0.39)	0.715	0.69 (0.46)	0.69 (0.46)	0.005
Age of psoriasis onset	22.38 (12.44)	21.53 (11.63)	0.071	21.77 (11.98)	21.82 (11.83)	0.004
Disease duration at treatment start	23.91 (12.50)	22.82 (11.51)	0.091	23.40 (12.31)	23.30 (11.71)	0.009
Psoriatic arthritis	0.24 (0.42)	0.30 (0.45)	0.138	0.25 (0.42)	0.27 (0.44)	0.046
Methotrexate co-therapy at treatment start	0.09 (0.29)	0.12 (0.33)	0.095	0.09 (0.29)	0.12 (0.32)	0.069
HLA-C*06:02 dosage	0.57 (0.56)	0.56 (0.57)	0.007	0.58 (0.56)	0.57 (0.56)	0.015
PC1	-0.00 (0.02)	-0.00 (0.02)	0.022	-0.00 (0.02)	-0.00 (0.02)	0.004
PC2	-0.00 (0.02)	0.00 (0.02)	0.029	-0.00 (0.02)	0.00 (0.02)	0.043
PC3	-0.00 (0.02)	0.00 (0.02)	0.050	-0.00 (0.02)	0.00 (0.02)	0.057
PC4	-0.00 (0.02)	-0.00 (0.02)	0.012	0.00 (0.02)	-0.00 (0.02)	0.024
PC5	0.00 (0.02)	-0.00 (0.02)	0.073	-0.00 (0.02)	-0.00 (0.02)	0.065

Table E5 – Significant interaction of drug and *HLA-C*06:02* status in achievement of PASI75, PASI90 and PASI100 response based on inverse probability of treatment weighting using the propensity score

	P	PASI75 response			PASI90 response			PASI100 response	
Interaction term	3 months	6 months	12 months	3 months	6 months	12 months	3 months	6 months	12 months
Drug × BL PASI									
Effect size (beta)	-0.025	0.038	-0.075	-0.067	0.047	-0.022	-0.030	0.052	0.012
95% CI	(-0.105, 0.055)	(-0.028, 0.105)	(-0.149, -0.001)	(-0.137, 0.003)	(-0.006, 0.100)	(-0.080, 0.035)	(-0.097, 0.037)	(-0.001, 0.105)	(-0.045, 0.069)
P-value	0.542	0.258	0.049	0.062	0.082	0.441	0.379	0.056	0.683
Drug × Age of Onset									
Effect size (beta)	0.006	-0.008	0.003	0.010	-0.008	0.006	0.031	0.011	0.000
95% CI	(-0.030, 0.043)	(-0.042, 0.026)	(-0.037, 0.042)	(-0.027, 0.047)	(-0.037, 0.021)	(-0.026, 0.037)	(-0.014, 0.077)	(-0.026, 0.048)	(-0.036, 0.036)
P-value	0.733	0.649	0.896	0.591	0.595	0.722	0.177	0.561	0.986
Drug × Disease Duration									
Effect size (beta)	0.028	0.000	0.003	0.021	-0.019	0.005	0.034	0.015	0.005
95% CI	(-0.008, 0.063)	(-0.032, 0.033)	(-0.032, 0.038)	(-0.016, 0.057)	(-0.049, 0.011)	(-0.027, 0.038)	(-0.011, 0.079)	(-0.024, 0.054)	(-0.032, 0.042)
P-value	0.131	0.987	0.851	0.270	0.205	0.747	0.141	0.458	0.788
Drug × PsA			X						
Effect size (beta)	-0.719	0.602	0.846	-0.310	0.128	0.912	-1.082	-0.258	0.588
95% CI	(-1.555, 0.117)	(-0.132, 1.336)	(0.008, 1.685)	(-1.240, 0.620)	(-0.589, 0.846)	(0.150, 1.673)	(-2.133, -0.030)	(-1.156, 0.640)	(-0.266, 1.442)
P-value	0.092	0.108	0.048	0.513	0.726	0.019	0.044	0.573	0.178
<i>HLA-C*06:02</i> × PsA) 7						
Effect size (beta)	-0.431	0.073	0.126	-0.774	-0.055	0.394	-0.409	-0.203	0.062
95% CI	(-1.156, 0.293)	(-0.572, 0.718)	(-0.593, 0.846)	(-1.492, -0.057)	(-0.672, 0.562)	(-0.233, 1.021)	(-1.230, 0.411)	(-0.906, 0.499)	(-0.619, 0.744)
P-value	0.244	0.825	0.731	0.035	0.862	0.218	0.329	0.571	0.858

HLA-C*06:02 × Biologic Naive									
Effect size (beta)	-0.134	0.426	0.372	-0.347	0.070	0.173	-0.320	-0.124	-0.114
95% CI	(-0.825, 0.558)	(-0.212, 1.064)	(-0.302, 1.045)	(-1.085, 0.391)	(-0.528, 0.668)	(-0.457, 0.803)	(-1.207, 0.566)	(-0.871, 0.623)	(-0.827, 0.599)
P-value	0.705	0.191	0.280	0.357	0.818	0.591	0.479	0.744	0.754
Drug × <i>HLA-C*06:02</i>						Q			
Effect size (beta)	-0.818	-1.205	-0.946	-0.893	-1.237	-0.988	-0.396	-1.217	-0.694
95% CI	(-1.535, -0.100)	(-1.860, -0.551)	(-1.607, -0.285)	(-1.616, -0.171)	(-1.818, -0.656)	(-1.585, -0.391)	(-1.284, 0.492)	(-1.911, -0.524)	(-1.326, -0.063)
P-value	0.026	3.24×10 ⁻⁴	5.16×10 ⁻³	0.016	3.32×10 ⁻⁵	1.23×10 ⁻³	0.382	6.05×10 ⁻⁴	0.032

Table E6 – Association of drug type with PASI75 and PASI100 response by *HLA-C*06:02* status

		PASI75 response			PASI100 response	
	3 months	6 months	12 months	3 months	6 months	12 months
HLA-C*06:02 Negative						
n adalimumab	195	265	243	195	265	243
n ustekinumab	113	153	137	113	153	137
n total	308	418	380	308	418	380
Drug: adalimumab vs ustekinumab						
Odds ratio	2.206	2.583	2.069	2.215	3.595	2.063
95% CI	(1.357, 3.585)	(1.671, 3.991)	(1.280, 3.346)	(1.133, 4.329)	(2.125, 6.082)	(1.274, 3.339)
P-value	1.41×10 ⁻³	1.93×10 ⁻⁵	3.02×10^{-3}	0.020	1.84×10 ⁻⁶	3.23×10 ⁻³
HLA-C*06:02 Positive						
n adalimumab	206	321	271	206	321	271
n ustekinumab	132	172	161	132	172	161
n total	338	493	432	338	493	432
Drug: adalimumab vs ustekinumab						
Odds ratio	1.171	1.055	1.146	1.325	0.963	0.931
95% CI	(0.726, 1.890)	(0.697, 1.598)	(0.728, 1.803)	(0.758, 2.315)	(0.627, 1.479)	(0.597, 1.451)
P-value	0.517	0.799	0.557	0.323	0.862	0.752

Table E7 – HLA-C*06:02 genotype associates with response to either drug

Statistics relate to *HLA-C*06:02* dosage term in separate multivariable models for response to adalimumab and ustekinumab. Other model covariates (ancestry PCs 1-5, baseline PASI, age of psoriasis onset, presence of psoriatic arthritis, biologic naive status, disease duration at treatment start and methotrexate co-therapy up to the response measurement date) not shown.

		Adalimumab		Ustekinumab			
	3 months	6 months	12 months	3 months	6 months	12 months	
n	401	586	514	245	325	298	
HLA-C*06:02 main effect: PASI75 response			1				
Effect size (OR)	1.059	0.775	0.802	2.624	1.856	1.675	
95% CI	(0.690, 1.625)	(0.544, 1.104)	(0.543, 1.183)	(1.530, 4.499)	(1.151, 2.993)	(0.997, 2.813)	
P-value	0.793	0.158	0.266	4.53×10 ⁻⁴	0.011	0.051	
HLA-C*06:02 main effect: PASI90 response			<i>></i>				
Effect size (OR)	0.972	0.544	0.782	2.702	1.722	1.864	
95% CI	(0.653, 1.447)	(0.397, 0.747)	(0.563, 1.085)	(1.520, 4.804)	(1.098, 2.699)	(1.170, 2.970)	
P-value	0.889	1.67×10 ⁻⁴	0.141	7.07×10 ⁻⁴	0.018	8.83×10 ⁻³	
HLA-C*06:02 main effect: PASI100 response							
Effect size (OR)	0.952	0.608	0.700	1.707	2.011	1.325	
95% CI	(0.601, 1.507)	(0.429, 0.863)	(0.490, 1.001)	(0.863, 3.374)	(1.157, 3.496)	(0.802, 2.189)	
P-value	0.834	5.35×10 ⁻³	0.051	0.124	0.013	0.272	

Table E8 – Association of drug type with PASI75 and PASI100 response by *HLA-C*06:02* and psoriatic arthritis status

		PASI75 response			PASI100 response	1
	3 months	6 months	12 months	3 months	6 months	12 months
HLA-C*06:02 Negative without PsA						
n adalimumab	124	159	160	124	159	160
n ustekinumab	83	109	93	83	109	93
n total	207	268	253	207	268	253
Drug: adalimumab vs ustekinumab			5			
Odds ratio	1.754	2.025	1.714	1.933	2.590	1.555
95% CI	(0.984, 3.125)	(1.178, 3.482) (0.936, 3.139)		(0.877, 4.260)	(1.387, 4.838)	(0.882, 2.743)
P-value	0.057	0.011	0.081	0.102	2.83×10 ⁻³	0.128
HLA-C*06:02 Negative with PsA						
n adalimumab	66	100	79	66	100	79
n ustekinumab	26	38	39	26	38	39
n total	92	138	118	92	138	118
Drug: adalimumab vs ustekinumab						
Odds ratio	5.329	4.841	3.281	4.142	8.866	4.436
95% CI	(1.946, 14.593)	(2.171, 10.793)	(1.419, 7.590)	(0.876, 19.583)	(2.550, 30.821)	(1.560, 12.614)
P-value	1.13×10 ⁻³	1.16×10 ⁻⁴	5.48×10 ⁻³	0.073	5.98×10 ⁻⁴	5.21×10 ⁻³
HLA-C*06:02 Positive without PsA		> , Y				
n adalimumab	150	231	198	150	231	198
n ustekinumab	91	128	115	91	128	115
n total	241	359	313	241	359	313
Drug: adalimumab vs ustekinumab						
Odds ratio	1.800	0.867	0.816	1.867	0.980	0.766
95% CI	(1.002, 3.236)	(0.529, 1.420)	(0.470, 1.418)	(0.947, 3.677)	(0.591, 1.624)	(0.454, 1.290)
P-value	0.049	0.571	0.471	0.071	0.937	0.315

HLA-C*06:02 Positive with PsA						
n adalimumab	47	82	65	47	82	65
n ustekinumab	35	37	41	35	37	41
n total	82	119	106	82	119	106
Drug: adalimumab vs ustekinumab						
Odds ratio	0.422	1.767	2.331	0.585	0.919	1.576
95% CI	(0.162, 1.097)	(0.771, 4.049)	(0.963, 5.644)	(0.189, 1.808)	(0.380, 2.220)	(0.634, 3.919)
P-value	0.077	0.178	0.061	0.351	0.851	0.327

Table E9 – Joint association of drug and biologic naive status with response

Results based on simple model that includes drug and biologic naive status terms, fitted using the full cohort of 1,326 patients (controlling for baseline PASI; no other covariate terms and in particular no interaction terms).

	P	ASI75 respons	se	PASI90 response			PASI100 response		
	3 months	6 months	12 months	3 months	6 months	12 months	3 months	6 months	12 months
n adalimumab	401	586	514	401	586	514	401	586	514
n ustekinumab	245	325	298	245	325	298	245	325	298
n total	646	911	812	646	911	812	646	911	812
Drug: adalimumab vs ustekinumab									
Effect size (beta)	0.262	0.311	0.218	0.442	0.204	-0.097	0.405	0.329	0.162
95% CI	(-0.104, 0.627)	(-0.002, 0.625)	(-0.129, 0.566)	(0.070, 0.813)	(-0.088, 0.496)	(-0.407, 0.214)	(-0.051, 0.860)	(-0.012, 0.671)	(-0.177, 0.501)
P-value	0.160	0.052	0.218	0.020	0.171	0.541	0.082	0.058	0.350
Biologic naive status									
Effect size (beta)	0.535	0.572	0.691	0.483	0.650	0.806	0.276	0.834	0.562
95% CI	(0.158, 0.911)	(0.249, 0.895)	(0.337, 1.045)	(0.087, 0.880)	(0.337, 0.963)	(0.472, 1.141)	(-0.207, 0.759)	(0.441, 1.227)	(0.184, 0.939)
P-value	5.38×10 ⁻³	5.23×10 ⁻⁴	1.32×10 ⁻⁴	0.017	4.80×10 ⁻⁵	2.29×10 ⁻⁶	0.263	3.14×10 ⁻⁵	3.54×10 ⁻³

Table E10 – Significant interaction of drug and *HLA-C*06:02* status in achievement of PASI90 response in biologic naive and biologic experienced subgroups

			PASI 90 i	esponse		
		Biologic naive		В	iologic experience	d
	3 months	6 months	12 months	3 months	6 months	12 months
n adalimumab	331	477	417	70	109	97
adalimumab responders	148 (44.7%)	253 (53.0%)	221 (53.0%)	20 (28.6%)	37 (33.9%)	36 (37.1%)
n ustekinumab	113	170	157	132	155	141
ustekinumab responders	36 (31.9%)	78 (45.9%)	91 (58.0%)	33 (25.0%)	52 (33.5%)	48 (34.0%)
n total	444	647	574	202	264	238
Drug × BL PASI interaction						
Effect size (beta)	-0.091	0.047	-0.056	-0.002	0.064	0.045
95% CI	(-0.179, -0.003)	(-0.007, 0.102)	(-0.138, 0.026)	(-0.137, 0.132)	(-0.035, 0.164)	(-0.056, 0.147)
P-value	0.042	0.088	0.182	0.972	0.203	0.380
Drug × Age of Onset interaction						
Effect size (beta)	0.007	-0.013	0.005	0.028	0.012	-0.002
95% CI	(-0.040, 0.054)	(-0.048, 0.022)	(-0.031, 0.041)	(-0.047, 0.103)	(-0.047, 0.071)	(-0.064, 0.061)
P-value	0.766	0.469	0.799	0.463	0.697	0.962
Drug × Disease Duration interaction						
Effect size (beta)	-0.002	-0.025	0.003	0.049	0.000	0.002
95% CI	(-0.049, 0.045)	(-0.061, 0.012)	(-0.035, 0.040)	(-0.019, 0.118)	(-0.059, 0.059)	(-0.055, 0.059)
P-value	0.935	0.182	0.890	0.157	0.992	0.949
Drug × PsA interaction						
Effect size (beta)	-0.424	-0.027	1.419	-0.172	0.350	-0.136
95% CI	(-1.803, 0.954)	(-1.050, 0.996)	(0.375, 2.462)	(-1.902, 1.559)	(-0.991, 1.690)	(-1.423, 1.151)
P-value	0.546	0.959	7.71×10 ⁻³	0.846	0.609	0.836

HLA-C*06:02 × PsA interaction						
Effect size (beta)	-0.834	0.088	0.349	-1.377	-1.031	0.298
95% CI	(-1.728, 0.059)	(-0.581, 0.757)	(-0.381, 1.079)	(-2.735, -0.019)	(-2.235, 0.174)	(-0.787, 1.383)
P-value	0.067	0.796	0.349	0.047	0.093	0.590
Drug × HLA-C*06:02 interaction				R		
Effect size (beta)	-0.655	-1.479	-0.963	-1.010	-1.038	-0.940
95% CI	(-1.594, 0.284)	(-2.189, -0.768)	(-1.673, -0.253)	(-2.484, 0.464)	(-2.224, 0.148)	(-2.071, 0.190)
P-value	0.171	4.58×10 ⁻⁵	7.87×10 ⁻³	0.179	0.086	0.103

Table E11 – Association of drug type with PASI90 response by *HLA-C*06:02* and psoriatic arthritis status in biologic naive and biologic experienced subgroups

N/A confidence interval for *HLA-C*06:02* negative and biologic naive patients with PsA at 3m is due to zero (of five) observed responders to ustekinumab.

		All		Sub	group without	PsA	Subgroup with PsA		
	3 months	6 months	12 months	3 months	6 months	12 months	3 months	6 months	12 months
HLA-C*06:02 Negative and biologic									
naive									
n adalimumab	161	215	194	105	126	128	51	83	62
n ustekinumab	54	77	69	46	65	56	5	8	11
n total	215	292	263	151	191	184	56	91	73
Drug: adalimumab vs ustekinumab									
Odds ratio	3.047	3.119	1.406	2.463	2.482	1.142	3.60×10 ⁷	14.452	4.418
95% CI	(1.444, 6.427)	(1.802, 5.400)	(0.805, 2.458)	(1.093, 5.550)	(1.322, 4.662)	(0.601, 2.172)	N/A	(1.680, 124.3)	(1.056, 18.492)
P-value	3.45×10 ⁻³	4.84×10 ⁻⁵	0.231	0.030	4.70×10 ⁻³	0.684	0.992	0.015	0.042
HLA-C*06:02 Positive and biologic									
naive			\triangle	/					
n adalimumab	170	262	223	124	189	166	38	66	50
n ustekinumab	59	93	88	42	71	64	13	16	19
n total	229	355	311	166	260	230	51	82	69
Drug: adalimumab vs ustekinumab			× , Y						
Odds ratio	1.154	0.669	0.470	1.514	0.857	0.314	0.469	0.282	1.008
95% CI	(0.629, 2.116)	(0.415, 1.077)	(0.278, 0.796)	(0.736, 3.117)	(0.495, 1.482)	(0.167, 0.592)	(0.125, 1.766)	(0.082, 0.967)	(0.332, 3.061)
P-value	0.644	0.098	4.93×10 ⁻³	0.260	0.580	3.42×10 ⁻⁴	0.263	0.044	0.989
HLA-C*06:02 Negative and biologic									
experienced									
n adalimumab	34	50	49	19	33	32	15	17	17
n ustekinumab	59	76	68	37	44	37	21	30	28
n total	93	126	117	56	77	69	36	47	45

Drug: adalimumab vs ustekinumab									
Odds ratio	1.817	1.570	1.773	1.495	1.381	1.831	2.233	1.810	1.466
95% CI	(0.618, 5.347)	(0.708, 3.479)	(0.781, 4.025)	(0.356, 6.288)	(0.505, 3.773)	(0.626, 5.355)	(0.412, 12.103)	(0.473, 6.929)	(0.359, 5.985)
P-value	0.278	0.267	0.171	0.583	0.529	0.269	0.351	0.386	0.594
HLA-C*06:02 Positive and biologic									
experienced									
n adalimumab	36	59	48	26	42	32	9	16	15
n ustekinumab	73	79	73	49	57	51	22	21	22
n total	109	138	121	75	99	83	31	37	37
Drug: adalimumab vs ustekinumab									
Odds ratio	1.010	0.769	0.921	0.996	0.693	0.801	1.290	1.076	0.785
95% CI	(0.432, 2.365)	(0.373, 1.588)	(0.430, 1.976)	(0.373, 2.656)	(0.303, 1.582)	(0.318, 2.018)	(0.182, 9.133)	(0.167, 6.938)	(0.168, 3.672)
P-value	0.981	0.478	0.833	0.993	0.384	0.638	0.799	0.939	0.759

Table E12 – HLA alleles with strongest evidence for interaction with drug

Based on full GxE model including clinical covariates and interaction terms. The ten most strongly associated HLA alleles are reported for each combination of outcome (PASI75, PASI90, PASI100) and time-point. "Interaction p-value": p-value of HLA allele dosage × Drug interaction term; "Conditional on HLA-C*06:02": the p-value for the same interaction term in a model that also includes HLA-C*06:02 main effect and interaction terms. *: P < 0.05; **: P < 0.005; **: P < 1.17×10⁻⁴ (Bonferroni multiple testing threshold for 142 alleles × 3 time-points = 426 tests). Table entries for HLA-C*06:02 are highlighted in bold underlined font; note that HLA-C*06:02 is not among the top ten alleles for PASI100 response at 3m.

		PASI75 response			PASI90 response	9	PASI100 response			
	Allele	Interaction p-value	Conditional on HLA-C*06:02	Allele	Interaction p-value	Conditional on HLA-C*06:02	Allele	Interaction p-value	Conditional on HLA-C*06:02	
	HLA-B*35:01	**4.96×10 ⁻³	*8.92×10 ⁻³	HLA-C*04	*5.45×10 ⁻³	*0.013	HLA-B*37	*0.016	*0.036	
	HLA-B*35	*5.32×10 ⁻³	*9.65×10 ⁻³	HLA-C*04:01	*5.45×10 ⁻³	*0.013	HLA-B*37:01	*0.016	*0.036	
	HLA-DRB1*01:01	*0.013	*9.25×10 ⁻³	HLA-B*35:01	*6.20×10 ⁻³	*0.008	HLA-DRB1*04:01	*0.025	*0.026	
	HLA- DQB1*05:01	*0.014	*0.012	HLA- DQB1*05:01	*0.010	*0.011	HLA-B*55:01	*0.039	*0.024	
3 months	HLA-C*04	*0.019	*0.047	HLA-B*35	*0.011	*0.015	HLA-DRB1*04	*0.049	*0.044	
	HLA-C*04:01	*0.019	*0.047	HLA-DRB1*01	*0.013	*0.013	HLA-DPB1*04:02	0.054	*0.045	
	HLA-DRB1*13:02	*0.026	*0.012	HLA-DQB1*05	*0.014	*0.010	HLA-DQB1*06	0.086	0.052	
	<u>HLA-C*06:02</u>	* <u>0.026</u>	N/A	HLA-C*06:02	* <u>0.017</u>	N/A	HLA-DRB1*13	0.089	0.060	
	HLA-DRB1*01	*0.048	*0.050	HLA-DRB1*01:01	*0.026	*0.022	HLA- DQB1*03:01	0.103	*0.045	
	HLA-DRB1*14:01	0.070	0.094	HLA-B*44	*0.032	**0.004	HLA- DQA1*03:01	0.112	0.083	
	Allele	Interaction p-value	Conditional on HLA-C*06:02	Allele	Interaction p-value	Conditional on HLA-C*06:02	Allele	Interaction p-value	Conditional on HLA-C*06:02	
	HLA-C*06:02	** <u>1.21×10⁻³</u>	N/A	HLA-C*06:02	*** <u>3.76×10⁻⁵</u>	N/A	HLA-C*06:02	** <u>5.00×10⁻⁴</u>	N/A	
	HLA- DQB1*03:03	**2.84×10 ⁻³	0.054	HLA-B*13:02	*0.012	0.249	HLA-B*37	*0.024	0.181	
	HLA-DRB1*01	*7.08×10 ⁻³	*0.015	HLA-B*13	*0.013	0.264	HLA-B*37:01	*0.024	0.182	
	HLA-	*7.85×10 ⁻³	0.205	HLA-B*37	*0.018	0.181	HLA-	0.051	0.562	

	DQA1*02:01						DQB1*03:03		
6 months	HLA-DRB1*07	*8.86×10 ⁻³	0.225	HLA-B*37:01	*0.018	0.181	HLA-DRB1*01:03	0.052	0.066
	HLA-DQA1*01	*8.87×10 ⁻³	*0.027	HLA-A*30:01	*0.022	0.063	HLA-C*04:01	0.054	0.139
	HLA-DRB1*07:01	*8.87×10 ⁻³	0.225	HLA-A*30	*0.032	0.069	HLA-C*04	0.054	0.139
	HLA- DQA1*01:01	*9.38×10 ⁻³	*0.021	HLA- DQB1*03:03	*0.040	0.766	HLA- DQA1*05:01	0.072	0.429
	HLA- DQB1*05:01	*9.39×10 ⁻³	*0.019	HLA-C*12	*0.045	0.192	HLA- DQB1*02:01	0.072	0.451
	HLA-DQB1*05	*9.54×10 ⁻³	*0.022	HLA-A*29	*0.046	0.058	HLA-B*13	0.075	0.635
	Allele	Interaction p-value	Conditional on HLA-C*06:02	Allele	Interaction p-value	Conditional on HLA-C*06:02	Allele	Interaction p-value	Conditional on HLA-C*06:02
	HLA-B*57:01	**2.17×10 ⁻³	*0.031	HLA-C*12	**4.95×10 ⁻⁴	**3.45×10 ⁻³	HLA-B*57	*9.11×10 ⁻³	0.082
	HLA-B*57	**4.65×10 ⁻³	0.056	HLA-B*57	**1.14×10 ⁻³	*0.035	HLA-C*02:02	*0.012	*9.24×10 ⁻³
	HLA-C*12	*5.95×10 ⁻³	*0.027	HLA-C*12:03	**1.33×10 ⁻³	*7.79×10 ⁻³	HLA-B*57:01	*0.014	0.126
	HLA-A*25:01	*7.31×10 ⁻³	*0.014	HLA-B*39	**1.53×10 ⁻³	*5.54×10 ⁻³	HLA-C*06:02	* <u>0.023</u>	N/A
12 months	HLA- DQB1*03:01	*8.38×10 ⁻³	*0.017	HLA-C*06:02	** <u>1.90×10⁻³</u>	N/A	HLA- DQB1*03:01	*0.027	*0.042
	HLA- DQB1*03:03	*0.011	0.083	HLA-B*57:01	**2.59×10 ⁻³	0.083	HLA-DRB1*13:01	*0.029	*0.021
	HLA-C*06:02	* <u>0.012</u>	N/A	HLA-DPA1*01:03	*0.016	*0.012	HLA-B*27	*0.042	*0.033
	HLA-C*12:03	*0.020	0.070	HLA-DPA1*01	*0.032	*0.023	HLA- DQA1*05:01	*0.044	0.147
	HLA-C*04:01	*0.032	0.063	HLA-DPA1*02	*0.032	*0.023	HLA-DRB1*07	*0.046	0.212
	HLA-C*04	*0.032	0.063	HLA-C*02:02	*0.036	*0.022	HLA-DRB1*07:01	*0.046	0.212

Table E13 – HLA alleles with strongest evidence for interaction with drug independently of *HLA-C*06:02*

Based on full GxE model including clinical covariates and interaction terms, plus HLA-C*06:02 main effect and interaction terms. The ten most strongly associated HLA alleles are reported for each combination of outcome (PASI75, PASI90, PASI100) and time-point. *: P < 0.05; **: P < 0.005; no tests achieved P < 1.17×10⁻⁴ (Bonferroni multiple testing threshold for 142 alleles × 3 time-points = 426 tests).

	PASI75 re	esponse	PASI90 re	sponse	PASI100 re	sponse
	Allele	Interaction p-value	Allele	Interaction p-value	Allele	Interaction p-value
	HLA-B*35:01	*8.92×10 ⁻³	HLA-B*44	**4.16×10 ⁻³	HLA-B*55:01	*0.024
	HLA-DRB1*01:01	*9.25×10 ⁻³	HLA-B*35:01	*8.28×10 ⁻³	HLA-DRB1*04:01	*0.026
	HLA-B*35	*9.65×10 ⁻³	HLA-DQB1*05	*0.010	HLA-B*37	*0.036
	HLA-DRB1*13:02	*0.012	HLA-DQB1*05:01	*0.011	HLA-B*37:01	*0.036
3 months	HLA-DQB1*05:01	*0.012	HLA-C*04:01	*0.013	HLA-DRB1*04	*0.044
	HLA-DPB1*13	*0.044	HLA-C*04	*0.013	HLA-DPB1*04:02	*0.045
	HLA-DPB1*13:01	*0.044	HLA-DRB1*13	*0.013	HLA-DQB1*03:01	*0.045
	HLA-DQB1*03:01	*0.045	HLA-DRB1*01	*0.013	HLA-DQB1*06	0.052
	HLA-C*04	*0.047	HLA-B*44:02	*0.015	HLA-DRB1*13	0.060
	HLA-C*04:01	*0.047	HLA-B*35	*0.015	HLA-B*44	0.073
	Allele	Interaction p-value	Allele	Interaction p-value	Allele	Interaction p-value
	HLA-DRB1*01	*0.015	HLA-DPB1*10:01	*0.037	HLA-DRB1*01:03	0.066
	HLA-C*01:02	*0.018	HLA-DPB1*10	*0.037	HLA-DRB1*15:01	0.090
	HLA-DQB1*05:01	*0.019	HLA-A*29	0.058	HLA-DRB1*15	0.091
	HLA-DQA1*01:01	*0.021	HLA-A*30:01	0.063	HLA-B*27	0.092
6 months	HLA-DQB1*05	*0.022	HLA-A*30	0.069	HLA-DQB1*06:02	0.093
	HLA-DQA1*01	*0.027	HLA-B*57	0.082	HLA-B*27:05	0.102
	HLA-DRB1*01:01	*0.038	HLA-DRB1*01:03	0.087	HLA-A*29:02	0.102
	HLA-DQB1*03:03	0.054	HLA-C*01:02	0.090	HLA-C*07	0.104

	HLA-DQB1*03	0.055	HLA-DQB1*06:02	0.095	HLA-A*29	0.105
	HLA-DQA1*01:03	0.077	HLA-A*29:02	0.100	HLA-C*07:01	0.122
	Allele	Interaction p-value	Allele	Interaction p-value	Allele	Interaction p-value
	HLA-A*25:01	*0.014	HLA-C*12	**3.45×10 ⁻³	HLA-C*02:02	*9.24×10 ⁻³
	HLA-B*13:02	*0.017	HLA-B*39	*5.54×10 ⁻³	HLA-DRB1*13:01	*0.021
	HLA-DQB1*03:01	*0.017	HLA-C*12:03	*7.79×10 ⁻³	HLA-B*27	*0.033
	HLA-B*13	*0.022	HLA-DPA1*01:03	*0.012	HLA-B*27:05	*0.037
12 months	HLA-C*12	*0.027	HLA-C*02:02	*0.022	HLA-DQA1*01:03	*0.038
	HLA-DQB1*06	*0.029	HLA-DPA1*01	*0.023	HLA-DQB1*06:03	*0.041
	HLA-B*57:01	*0.031	HLA-DPA1*02	*0.023	HLA-DQB1*03:01	*0.042
	HLA-DRB1*04:01	*0.048	HLA-B*57	*0.035	HLA-DPA1*02:02	0.055
	HLA-DQA1*01:02	0.053	HLA-DPA1*02:02	*0.040	HLA-A*31:01	0.058
	HLA-DQA1*01	0.054	HLA-A*68:01	*0.046	HLA-A*31	0.058

Table E14 – Full drug × HLA allele interaction test results for all HLA alleles

See supplementary data file (Excel workbook)



Table E15 – GxGxE test results for interaction between HLA-C*06:02 and ERAP1 variant rs27524

Based on full GxGxE model including the second-order interaction term drug × *HLA-C*06:02* dosage × rs27524 genotype, all lower-order interaction and main-effect terms, and all covariates from the full GxE model. Results shown are for first- and second-order interaction terms between drug, *HLA-C*06:02* dosage and rs27524 genotype only.

		PASI75 response			PASI90 response			PASI100 response	
	3 months	6 months	12 months	3 months	6 months	12 months	3 months	6 months	12 months
n adalimumab	401	586	514	401	586	514	401	586	514
n ustekinumab	245	325	298	245	325	298	245	325	298
n total	646	911	812	646	911	812	646	911	812
Drug × HLA-C*06:02 interaction									
Effect size (beta)	-1.201	-0.649	-0.744	-0.634	-1.304	-0.674	-0.419	-1.195	-0.597
95% CI	(-2.274, -0.127)	(-1.559, 0.262)	(-1.713, 0.225)	(-1.700, 0.432)	(-2.140, -0.469)	(-1.499, 0.151)	(-1.722, 0.884)	(-2.182, -0.207)	(-1.513, 0.318)
P-value	0.028	0.163	0.132	0.243	2.22×10 ⁻³	0.109	0.528	0.018	0.201
Drug × rs27524 interaction									
Effect size (beta)	-0.751	0.301	-0.101	0.092	-0.017	-0.209	-0.410	-0.234	-0.264
95% CI	(-1.484, -0.019)	(-0.370, 0.972)	(-0.844, 0.642)	(-0.746, 0.929)	(-0.655, 0.622)	(-0.871, 0.453)	(-1.389, 0.569)	(-1.013, 0.545)	(-0.986, 0.458)
P-value	0.044	0.379	0.789	0.830	0.959	0.536	0.412	0.556	0.473
HLA-C*06:02 × rs27524 interaction			X						
Effect size (beta)	-0.422	0.314	0.090	0.078	-0.331	0.053	0.027	-0.109	0.060
95% CI	(-1.177, 0.333)	(-0.370, 0.998)	(-0.636, 0.815)	(-0.723, 0.879)	(-0.985, 0.323)	(-0.597, 0.703)	(-0.904, 0.957)	(-0.902, 0.683)	(-0.648, 0.768)
P-value	0.274	0.368	0.809	0.848	0.321	0.873	0.955	0.787	0.868
Drug × <i>HLA-C*06:02</i> × rs27524 interaction) '						
Effect size (beta)	0.585	-0.506	-0.131	-0.312	0.090	-0.259	0.028	0.013	-0.102
95% CI	(-0.339, 1.509)	(-1.343, 0.332)	(-1.039, 0.777)	(-1.257, 0.632)	(-0.702, 0.883)	(-1.059, 0.540)	(-1.066, 1.122)	(-0.923, 0.949)	(-0.971, 0.767)
P-value	0.215	0.237	0.778	0.517	0.823	0.525	0.960	0.979	0.818

Table E16 – GxE model for drug and ERAP1 genotype among patients that are HLA-C*06:02 negative

Based on GxE model for patients that are *HLA-C*06:02* negative only. Results are presented for the model interaction term only. Results for other model terms are not shown; in particular main effect terms are not unambiguously interpretable in the presence of an interaction term.

	P	PASI75 response			PASI90 response			PASI100 response		
	3 months	6 months	12 months	3 months	6 months	12 months	3 months	6 months	12 months	
HLA-C*06:02 Negative						7				
n adalimumab	195	265	243	195	265	243	195	265	243	
n ustekinumab	113	153	137	113	153	137	113	153	137	
n total	308	418	380	308	418	380	308	418	380	
Drug × rs27524 interaction										
Effect size (beta)	-0.893	0.082	-0.346	0.166	-0.109	-0.319	-0.410	-0.356	-0.314	
95% CI	(-1.644, -0.142)	(-0.594, 0.758)	(-1.086, 0.393)	(-0.732, 1.064)	(-0.771, 0.552)	(-0.986, 0.349)	(-1.437, 0.616)	(-1.171, 0.459)	(-1.049, 0.422)	
P-value	0.020	0.812	0.359	0.717	0.746	0.350	0.433	0.392	0.403	

Table E17 – Test results for HLA-C*06:02 and ERAP1 model excluding GxGxE term

Based on model including same main effect and first-order interaction terms as the full GxGxE model, but no second-order interaction term. Results shown are for interaction terms between drug, *HLA-C*06:02* dosage and rs27524 genotype only.

		PASI75 response			PASI90 response		PASI100 response		
	3 months	6 months	12 months	3 months	6 months	12 months	3 months	6 months	12 months
n adalimumab	401	586	514	401	586	514	401	586	514
n ustekinumab	245	325	298	245	325	298	245	325	298
n total	646	911	812	646	911	812	646	911	812
Drug × HLA-C*06:02 interaction									
Effect size (beta)	-0.722	-1.051	-0.845	-0.886	-1.235	-0.863	-0.395	-1.185	-0.675
95% CI	(-1.470, 0.025)	(-1.680, -0.422)	(-1.522, -0.167)	(-1.639, -0.133)	(-1.813, -0.657)	(-1.451, -0.275)	(-1.292, 0.502)	(-1.866, -0.504)	(-1.308, -0.043)
P-value	0.058	0.001	0.015	0.021	2.80×10 ⁻⁵	4.01×10 ⁻³	0.388	6.45×10 ⁻⁴	0.036
Drug × rs27524 interaction									
Effect size (beta)	-0.440	0.010	-0.177	-0.115	0.037	-0.363	-0.392	-0.226	-0.324
95% CI	(-0.979, 0.098)	(-0.454, 0.473)	(-0.703, 0.349)	(-0.668, 0.439)	(-0.397, 0.470)	(-0.825, 0.098)	(-1.054, 0.270)	(-0.740, 0.287)	(-0.832, 0.183)
P-value	0.109	0.968	0.510	0.685	0.868	0.123	0.246	0.388	0.210
<i>HLA-C*06:02</i> × rs27524 interaction			X						
Effect size (beta)	-0.030	-0.022	0.007	-0.145	-0.270	-0.118	0.047	-0.100	-0.007
95% CI	(-0.470, 0.409)	(-0.417, 0.372)	(-0.435, 0.448)	(-0.572, 0.281)	(-0.642, 0.102)	(-0.498, 0.263)	(-0.449, 0.543)	(-0.524, 0.323)	(-0.422, 0.407)
P-value	0.892	0.912	0.976	0.504	0.155	0.545	0.853	0.642	0.973

Table E18 – GxE test results for which duplicated patients are excluded from both groups

Results of fitting the simple GxE model including covariate terms for baseline PASI, five ancestry PCs, drug, *HLA-C*06:02* dosage and the drug × *HLA-C*06:02* interaction, after excluding 101 patients that were randomly allocated to adalimumab/ustekinumab groups due to having eligible records for both. Results are comparable to main findings shown in Table E2.

	PASI75 response			P	PASI90 response			PASI100 response		
	3 months	6 months	12 months	3 months	6 months	12 months	3 months	6 months	12 months	
n adalimumab	379	548	489	379	548	489	379	548	489	
n ustekinumab	216	294	268	216	294	268	216	294	268	
n total	595	842	757	595	842	757	595	842	757	
Drug × HLA-C*06:02 interaction										
Effect size (beta)	-0.794	-0.972	-0.846	-1.108	-1.177	-0.813	-0.794	-1.227	-0.804	
95% CI	(-1.454, -0.135)	(-1.560, -0.384)	(-1.476, -0.216)	(-1.802, -0.414)	(-1.718, -0.636)	(-1.360, -0.266)	(-1.612, 0.024)	(-1.873, -0.582)	(-1.405, -0.204)	
P-value	0.018	1.21×10 ⁻³	8.53×10 ⁻³	1.75×10 ⁻³	2.03×10 ⁻⁵	3.56×10 ⁻³	0.057	1.95×10 ⁻⁴	8.68×10 ⁻³	

Supplementary Methods

Genotype data and HLA imputation

DNA was isolated from blood using standard methods. Genotyping was performed using Illumina HumanOmniExpressExome-8 v1.2 and v1.3 BeadChips. Three rounds of genotype calling were performed using Illumina's GenomeStudio Data Analysis software, based on four different genotyping batches (samples clustered using GenTrain 2.0 algorithm). Genotyping QC was performed using PLINK v1.07 1 , KING v1.4 2 and R 3 . Samples were excluded based on call rate (<0.99), mismatch with recorded gender, heterozygosity (±4 s.d. from the mean), relatedness (second degree relative or closer; kinship coefficient > 0.0884), suspected non-European ancestry indicated by principal component analysis (PCA) and residual PCA outlier status (>5 s.d. from the mean for PCs 1-20). Genetic variants were excluded based on call rate (<0.99), low GenomeStudio cluster separation score (<0.4), deviations from Hardy-Weinberg equilibrium (P < 7.5×10 $^{-8}$ based on number of variants tested) and minor allele frequency <1%. To eliminate potential batch effects we checked that there were no allele flips between batches and excluded variants with differential missing rates (P < 0.01) and allele frequencies (P < 10 $^{-5}$; 7 variants) between batches.

HLA imputation proceeded as follows. First, genotype intensity cluster plots were inspected for 3,141 single nucleotide polymorphisms in the HLA region (all SNPs within the range chr6:29494897-33160425 in the GRCh37/hg19 genome assembly, to correspond to the imputation reference panel described below). Where appropriate, genotypes were manually "rescued" using Evoker (version 2.3)⁴. Classical HLA alleles were imputed using SNP2HLA (v1.0.3), based on the T1DGC reference panel⁵. We excluded poorly imputed alleles (R2 < 0.9) and alleles with frequency <0.01, giving a total of 142 distinct 2- and 4-digit imputed alleles.

Statistical modelling

To generate the full multivariable logistic regression model for response accounting for potential clinical confounders, main effect and interaction covariate terms were added based on correlations with *HLA-C*06:02* or drug (**Table 1**). For variables significantly correlated with *HLA-C*06:02*, an interaction term with drug was included, and vice versa.

The full model included: covariate main effect terms for baseline PASI, ancestry PCs 1-5 derived from 108,319 independent SNPs using KING software², age of psoriasis onset, presence of PsA, biologic naive status, disease duration at treatment start, and methotrexate co-therapy up to the response measurement date (binary variable); interaction terms with drug for age of onset,

baseline PASI, disease duration and PsA; and interaction terms with *HLA-C*06:02* dosage for PsA and biologic naive status

Propensity score modelling

To confirm that our full multivariable model adequately controlled for potential confounding via covariates influencing treatment selection, we repeated the regression analysis with inverse probability of treatment weighting (IPTW) using the propensity score⁶. Specifically, we derived a propensity score model to estimate the probability that each patient would have been received treatment with adalimumab rather than ustekinumab. As recommended by Austin⁶, we included in the propensity score model all "potential confounders": covariates that were independently associated with PASI90 response. Conservatively, we included all covariates that demonstrated a nominal association with PASI90 response (P < 0.05) at any of our three time-points, among adalimumab patients only, ustekinumab patients only, or all patients combined (data not shown). The propensity score model included baseline PASI, ancestry PC 1, age of psoriasis onset, presence of PsA, biologic naive status, disease duration at treatment start and *HLA-C*06:02* dosage. Balance analysis showed that all covariates were well matched between adalimumab and ustekinumab groups after IPTW using the propensity score (**Table E4, Figure E1**): all standardised mean differences were below the accepted threshold of 0.1 at which a covariate differences between groups can be considered negligible⁶.

IPTW can be incorporated into regression models analogously to survey sampling weights. The full multivariable logistic regression model (described in the previous section) was re-fitted using IPTW derived from the propensity score model using the 'survey' package in R.

References for supplementary methods

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Supplementary Data

HLA-C*06:02 genotype is a predictive biomarker of biologic treatment response in psoriasis vulga

Nick Dand, Michael Duckworth, David Baudry, Alice Russell, Charles J. Curtis, Sang Hyuck Lee, Ian Evans, Kayleigh J. Ma BADBIR study group, Ali Alsharqi, Gabrielle Becher, A. David Burden, Richard G. Goodwin, Kevin McKenna, Ruth Murph Gayathri K. Perera, Radu Rotarescu, Shyamal Wahie, Andrew Wright, Nick J. Reynolds, Richard B. Warren, Christopher Griffiths, Catherine H. Smith*, Michael A. Simpson*, and Jonathan N. Barker*, on behalf of the BSTOP study group and

Table 114 Annual State Control of the Control of th

Yull model": based on full Gall model including clinical covariates and interaction terms; "Conditional on HEA-C*06/02": based on a model that also includes HEA-C*06/02 main

	PASST response 3m 4m 12m								98330 response 2m 6m 12m									PASIIO response 2m 6m 12m															
	Full model drug Beta	x HLA allele interaction Sil	Conditional of Beta	on HLA-C*06/02 Si	Full model drug P Bets	aultscratis elella A.M×g	Conditional on HLA-C*D Sets Si	i OZ Full el	odel drug = NLA allele interacti Beta SS	n Conditional or	HLA-C*06:02	Full model drug × H.A Reta	data interaction	Conditional on HLA-C Beta S	*66:82 £ P	ull model drug + MLA silele lieta Si	deraction Con	ditional on MLA-C*05:00	Full model di P Beta	ing x HLA allele interac Si	ction Con	nditional on HLA-C*06:02	Full model drug v	NLA affele interaction Sil	Conditional on HLF P Beta	1-C*06:02 F	uli model drug x HLA si Beta	belle interaction	Conditional on HLA-C*	Oli 02 Full mode P Si	el drug × HLA adole inter	saction 6	conditional on HLA-C*06:02 Seta SE P
ALA-4*00:01 ALA-4*00:01		0.3263 0.35 0.3264 0.35 0.3087 0.35	0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0	0.8390 0.37 0.3391 0.37 0.3185 0.69	722 -0.1768 795 -0.1699 127 -0.1891	0.2717 0.5296 0.2716 0.5559 0.2565 0.6611	100 100	0.9012 0.9292 0.3590	1.000 0.3097 1.200 0.3097 1.2060 0.2827	0.2756 -0.2065 0.2866 -0.3062 0.6662 0.3050	0.0140	0.0451 0 0.0451 0	1206 0.9000 1208 0.8881 1129 0.6980	0.2727 0.335 0.2781 0.335 -0.1653 0.319	6 0.6158 6 0.6078 0 0.6487	0.0654 0.2529 0.0892 0.2581 0.1218 0.2855	0.000 0.00	1	0.5865 -0.2869 0.6996 -0.0965	0.3744 0.3744 0.3828	STATE STAT	1	1.6154 0.0524 1.6154 0.3106	0.3917 0.6 0.3917 0.6 0.3973 0.6		064 0.6222 968 0.6222	-0.1282 0.3 -0.1182 0.3 -0.1182 0.3	965 0.2585 964 0.2585 778 0.6705	-0.1686 0.8000 -0.1614 0.8000 -0.1777 0.2808	0.6142 -0.01 0.6142 -0.01	07 0.2968 95 0.2966 08 0.2668	0.8118 0 0.7887 0 0.6198 0	1997 1997
ALA-A*02:01 ALA-A*02	-0.0008 0.3813	0.3123 0.56 0.5011 0.66	69 -0.2985 05 0.3166	0.3201 0.90 0.5109 0.53	60 -0.1016 50 -0.1696	0.2556 0.6079 0.8605 0.7552	0.1796 0.2600 0.1127 0.4690	0.5666 0.8077	12069 0.2840 16857 0.5503	0.3867 0.3697 0.3128 -0.6800	0.3964 0.3947 0.5537 0.3196	-0.0795 0 -0.0245 0	2156 0.8036 5238 0.9628	-0.1091 0.322 -0.0081 0.535	6 0.7691 2 0.9680	0.0539 0.2358 0.2450 0.3980	0.8091 -0.09 0.5448 0.25	02 0.2388 25 0.4021	0.7056 -0.0613 0.5300 -0.1345	0.3841	0.8019 -0.07 0.7816 -0.16	93 0.2666 13 0.3938	1.7509 0.4310 1.6921 -0.2410	0.3950 0.1 0.6029 0.6	2752 0.6153 0.9 6896 0.296 0.6	974 0.2779 088 0.6929	-0.0882 0.3 0.5780 0.4	291 0.8680 988 0.3661	-0.1028 0.2821 0.6475 0.5065	0.7156 0.10 0.2011 0.20	169 0.2680 178 0.6530	0.6966 0 0.6650 0	0918 0.2690 0.7230 1660 0.6526 0.7138
MAA-4-11:01	0.6581	0.6060 0.21 0.6070 0.21	73 0.3925 67 0.4120	0.6238 0.52 0.6247 0.50	90 0.8024 96 0.8062	0.5186 0.1369 0.5188 0.1355	0.7200 0.5400 0.7216 0.5401	0.1867	17592 0.6353 17569 0.6357	0.2321 0.6005 0.2338 0.6080	0.6094 0.3672 0.6098 0.3096	0.5411 0 0.5706 0	6935 0.4353 6935 0.4130	02691 0790	6 0.7292 3 0.7202	0.6125 0.5097 0.6100 0.5099	0.9950 -0.58 0.9951 -0.58	64 0.5189 68 0.5191	0.2560 -0.7564 0.2580 -0.7290	0.5589	0.1999 -0.91	31 0.5736 57 0.5738	1.1116 -0.1605 1.1106 -0.1667	09407 04 09409 04	8645 0.4034 0.9 8592 0.4095 0.9	303 0.6776 693 0.6736	-0.5758 0.5 -0.5767 0.5	927 0.3317 929 0.3308	-0.7904 0.6065 -0.7922 0.6068	02289 -0.29	64 0.6027 67 0.6028	0.1800 -0	9085 0.6071 0.1867 9087 0.6072 0.1862
ALA-A*22 ALA-A*22:01	0.9517 0.9515	1.1714 0.41 1.1713 0.41	65 0.9794 66 0.9792	12327 0.42 12327 0.42	0.6952 0.6955	0.9765 0.6162 0.9765 0.6160	0.4799 0.9981 0.4902 0.9982	0.6272	.7930 1.2836 .7935 1.2837	0.1626 1.996 0.1626 1.8000	1,2999 0,1663 1,2999 0,1662	0.0904 1 0.0875 1	1013 0.9366 1012 0.9366	0.0793 1142 0.0790 1142	2 0.9459 2 0.9476	0.1806 0.9200 0.1805 0.9200	0.6759 0.30 0.6758 0.30	94 0.9226 95 0.9226	0.7976 2.5677 0.7979 2.5678	1.8605 1.8605	0.0590 2.651 0.0590 2.651	57 1.2700 58 1.2700	10526 -0.6765 10526 -0.6765	11351 05 11351 05	5511 0.7155 1.1c 5512 0.7155 1.1c	627 0.5912 627 0.5912	15461 13 15462 13	190 0.3052 190 0.3052	1.469 1.2171 1.469 1.2171	0.234N 0.96 0.234N 0.95	1.40% 120 1.40%	0.6900 0	9775 1.4127 0.6890 9852 1.4134 0.6858
ALA-A*3E02	0.6672	0.7797 0.40	65 -0.7272 47 -0.7997	0.7957 0.36	68 -0.2203 56 -0.2652	0.5754 0.6998 0.5854 0.6753	0.4277 0.5820 0.4580 0.5962	0.6626	12117 0.7028 12970 0.7204	0.7969 -0.2990 0.7969 -0.2957	0.7101 0.6799 0.7283 0.6948	-0.2524 0 -0.2755 0	7689 0.7266 7738 0.7258	-0.8965 0.770 -0.8105 0.802	0 0.6157	0.2988 0.5122 0.8255 0.5280	0.5600 0.10	67 0.5192 12 0.5347	0.8970 0.2168	0.5977	0.7199 0.12 0.6972 0.16	71 0.608 1 71 0.6247	1.8321 0.6609 1.8126 0.6557	0.9094 0.1 0.9529 0.4	5970 0.4477 0.90 6925 0.4208 0.90	284 0.6296 366 0.6666	0.6429 0.6 0.6605 0.6	512 0.3235 307 0.3247	0.5298 0.6617 0.5861 0.6812	0.6244 0.44	03 0.6426 88 0.6670	0.5001 0 0.5000 0	3651 0.6431 0.5702 3792 0.6675 0.5700
ALA-A*26 ALA-A*26:01	-0.0873 -0.0759	1.8806 0.56 1.8852 0.96	96 0.4337 63 0.4667	1.4299 0.76 1.4335 0.75	25 -0.7756 50 -0.8075	1.0625 0.6579 1.0525 0.6636	0.9434 1.0661 0.9788 1.0766	0.8962	15288 1.2758 1.4862 1.2915	0.6785 0.3014 0.7066 0.2590	1.81% 0.8190 1.8389 0.8860	-0.1309 1 -0.1299 1	2722 0.9186 2768 0.9186	0.4020 1269 0.4044 1270	9 0.7509	0.0644 1.0991 0.0538 1.0985	0.9530 -0.03	00 1.1165 80 1.1220	0.9786 2.0912 0.9730 2.0967	1.4167 1.4255	0.1999 2.256 0.1492 2.245	09 1.4356 07 1.4436	0.3169 -0.7669 0.3185 -0.7683	13929 03 13925 03	5902 -0.4758 1.in 5897 -0.4791 1.in	611 0.7266 659 0.7257	-0.5359 1.1 -0.5509 1.1	261 0.6342 318 0.6268	-0.6050 1.1059 -0.6058 1.1009	0.5760 23.76 0.5716 22.96	ikk 36.1474 45 36.7105	0.5109 18 0.5311 17	1586 36.6683 0.6203 2871 87.1250 0.6626
MLA-A*29 MLA-A*29:02	0.1887 0.1509 0.4690	0.8964 0.85 0.8962 0.86 0.9961 0.61	69 -0.2074 51 -0.1197 09 0.5473	0.8311 0.80 0.9108 0.90 0.9197 0.55	09 1.1100 02 0.2699 51 0.2156	0.6608 0.0918 0.6905 0.2685	0.8218 0.6668 0.8218 0.6998	0.0999	10970 0.7961 13064 0.8621	0.9015 0.0548 0.7177 -0.8507	0.7954 0.9655 0.8568 0.6826 0.7963 0.9855	02513 0 -02243 0 03053 0	7928 0.7558 8369 0.9768 8959 0.9167	-0.0673 0.022 -0.2552 0.059 0.3477 0.030	7 0.9366 5 0.7665 9 0.7065	1.2791 0.6403 1.1073 0.6637 1.6987 0.7999	0.0899 1.22 0.0952 1.10 0.0917 -1.66	66 0.6719 80 0.7973	0.0980 0.6329 0.0998 0.4613 0.0698 1.2784	0.8883	0.3577 0.60 0.5332 0.42 0.1236 1.69	0.6978 1 20 0.7189 1	1.3962 -0.0226 1.5568 -0.1877 1.0687 -0.9391	10093 03 10093 03	9819 -0.1810 0.9 8529 -0.3085 1.0 4351 0.9130 1.0	968 0.8559 256 0.7636 579 0.4650	1.2866 0.3 1.3996 0.6	099 0.0862 084 0.0975 621 0.1996	1.2366 0.7606 1.3283 0.8136 0.6915 0.6965	0.1025 -0.61	05 0.7358 05 0.7569 06 1.560	0.5678 -0 0.5290 -0 0.9579 0	6706 0.7829 0.5216 5286 0.7568 0.6871 1636 11679 0.9878
ML4-A*32 ML4-A*32:01	-0.6127 0.6009	1.4179 0.66 1.1548 0.60	57 0.1628 32 0.3993	1.098 0.90 1.2061 0.76	65 -0.3969 66 0.1970	1.0123 0.6965 0.8664 0.8202	0.1604 1.0929 0.1644 0.8706	0.8966	1234 0.8840 16966 1.1065	0.6396 0.5290 -0.9513	0.9128 0.4835 1.1318 0.4006	-1.0792 1 -2.4099 1	2149 0.3748 6451 0.0954	-0.3942 1.259 -2.4101 1.478	6 0.7536 6 0.1090	-2.8164 1.2271 0.3411 0.8823	0.0217 -2.81 0.6991 0.86	k1 1,347k k2 0,8869	0.0690 1.3813 0.6946 -0.0683	1.0705 1.0709	0.1969 1.97 0.8690 -0.31	71 1.0990 94 1.0%4	1.0750 -1.4760 1.7667 -1.2441	5,9400 63 1,6494 64	2886 -1.0968 1.6 6890 -1,1950 1.6	126 0.4976 364 0.4754	-1.1167 1.6 -0.3118 1.6	014 0.3648 930 0.7628	-0.5211 1.0230 -0.3586 1.0268	0.6105 0.31 0.7268 -2.16	10 1.699 36 1.2413	0.8209 0 0.0856 -2	8625 1.6306 0.6050 3619 1.2369 0.0583
ALA-A*32:01 ALA-A*62	0.9699	0.7792 0.21 1.2397 0.30	26 0.9909 06 0.3348	07910 021 17710 079	03 -0.5100 60 -0.5100	0.7671 0.5006 0.7671 0.7047	0.1690 0.870s 0.8286 0.7649 0.2777 0.9659	0.2910	1.1222 0.6715 1.1223 0.6715	0.8555 -0.0753 0.8577 -14.6000 #	0.6841 0.9129 0.6841 0.9129	-0.0728 0 -0.0728 0	8202 0.9293 8203 0.9293	-0.1289 0.861 -0.1289 0.861	6 0.8868 6 0.8868	0.8625 0.8628 0.8687 0.7629 0.7734 0.7657	0.6000 -0.66	66 0.7766 16 0.7766	0.3919 -0.0927 0.7949 -1.9979	0.7299	03088 -0.26	18 0.7522 1	1.7278 -1.1823 1.7278 -1.1823	12186 03	2010 -E1908 1.6 2019 -E1961 1.2 5766 0.0000 1.70	568 0.4771 687 0.3962 699 0.4799	-0.8116 1.0 -0.8779 0.6 0.6784 0.6	542 0.6592 791 0.3657	-0.6505 0.8826 1.0729 0.9967	0.0610 0.10	66 1,2434 69 0,7298 66 0,976	0.8809 0	9651 1.2971 0.0580 0162 0.7973 0.9625 6784 0.9657 0.4434
ALA-4"68:01 ALA-8"07	0.1696 0.1668	1.2262 0.86 0.4802 0.75	00 0.0895 14 0.0969	1.2648 0.94 0.8900 0.94	0.6112 00 0.5413	0.9778 0.6741 0.4483 0.2272	0.6927 0.9968 0.9622 0.6571	0.6629 -5 0.6281 -	17972 418.9727 10777 0.5012	0.9718 -14.7920 4 0.8769 -0.2792	15.2784 0.9716 0.5110 0.5929	-0.2089 1 0.6705 0	1544 0.8591 5690 0.2387	-0.4671 1164 0.5231 0.585	2 0.7000	0.4055 0.8068 0.4059 0.4411	0.6052 0.89 0.8576 0.20	0.6170 80 0.4486	0.6911 -2.3512 0.6509 0.3663	1.3096 0.4152	0.0529 -2.439 0.3521 0.36	92 1.2297 179 0.4296	0.002 -0.008 0.002 -0.002	13600 04 07971 03	4722 -1.1362 1.8: 3941 0.5365 0.7:	125 0.3858 568 0.4784	0.9712 0.5 0.5360 0.5	900 0.2966 983 0.3703	1.0066 0.9420 0.3461 0.6086	0.2852 -0.91 0.5696 0.31	09 0.9066 64 0.6821	0.2962 -0 0.6629 0	9488 0.9169 0.3008 2010 0.4895 0.6369
MEA-8*07-02 MEA-8*08 MEA-8*0901	0.1695 0.3088 0.3088	0.4929 0.36 0.4927 0.62 0.4327 0.62	17 0.0660 96 -0.066 95 -0.066	0.5012 0.89 0.6534 0.98	62 0.3761 60 0.1667 60 0.1667	0.6612 0.6168 0.3536 0.6616 0.9536 0.6616	0.2056 0.6698 0.1729 0.8788 0.1729 0.8788	0.6616	12240 0.5165 1.1689 0.4228	0.6665 -0.4290 0.7247 -0.1305	0.5269 0.4221 0.4620 0.3672 0.4630 0.3675	0.6539 0 0.6025 0 0.6025 0	5798 0.4382 6688 0.3906 6689 0.3906	0.3356 0.595 0.1985 0.488 0.1985 0.488	2 0.5728 9 0.6867 9 0.6867	0.2557 0.6898 0.0989 0.3369 0.0981 0.3369	0.56990 0.06 0.7690 -0.29 0.7697 -0.19	19 0.4577 15 0.3543 14 0.3543	0.8925 0.2966 0.4049 0.0085 0.4049 0.0095	0.4182	0.8922 0.000	92 0.4268 1 35 0.4066 1	1.8962 0.9062 1.4407 0.7628	02581 01 06681 01	5051 0.6267 0.74 2538 0.6961 0.60 1539 0.6061 0.60	664 0.5795 892 0.3096 892 0.3096	0.4077 0.6 0.1027 0.3 0.1039 0.3	022 0.6986 970 0.7958 970 0.7958	0.2998 0.6190 -0.2928 0.6164 -0.7929 0.4164	0.6957 0.31	90 0.6920 76 0.6397 77 0.4397	0.5096 0 0.1239 0 0.1239 0	2909 0.6891 0.6968 4760 0.6530 0.2934 4760 0.4530 0.7533
MLA-8*1202	-0.9462 -0.9570	0.6784 0.36 0.6817 0.36	60 -0.3570 06 -0.3566	07370 0.62 07388 0.63	90 -1.2051 112 -1.2116	0.5632 0.0326 0.5632 0.0315	0.6789 0.6011 0.6921 0.6009	0.2615	17966 0.5709 18286 0.5817	0.1970 1.4270 0.1549 1.5124	0.6210 0.0216 0.6308 0.0165	-0.5836 0 -0.5708 0	6320 0.3558 6370 0.3702	0.0924 0.676 0.0546 0.678	8 0.9617	-1.1660 0.6682 -1.1822 0.6694	0.0128 -0.56 0.0118 -0.58	15 0.5025 36 0.5092	0.3688 0.8528 0.3686 0.4518	0.5054 0.5177	0.8851 0.96 0.8828 1.07	05 0.5422 06 0.5549	0.5380	87651 84 87757 83	4709 0.9629 0.71 3786 1.1201 0.80	958 0.2268 288 0.1787	-0.9128 0.5 -0.8983 0.5	119 0.0766 115 0.0790	-0.3620 0.5518 -0.2506 0.5512	0.6989 -0.20 0.6899 -0.23	90 0.543s 165 0.5698	0.7027 0 0.6806 0	2368 0.5832 0.6847 2024 0.6034 0.7974
MEA-8*16 MEA-8*16:02	-0.8905 -1.0279 0.7730	0.9245 0.50 0.9547 0.30 0.5213 0.60	19 -0.6666 16 -1.1678 10 0.1708	0.8662 0.59 0.9942 0.21 0.550n 0.34	95 -0.3982 92 -0.9032 93 0.4927	0.6917 0.5592 0.8709 0.2997 0.8909 0.79515	-0.50% 0.66% -1.0987 0.87% 0.6761 0.8961	0.000	13612 0.9992 15171 1.5958	0.1909 -0.8207 0.1167 -2.6120 0.1909 -0.1906	0.9293 0.7900 1.5769 0.0976 0.6040 0.6600	1,6065 1 1,7724 1 0,2113 0	0922 0.5459 3499 0.5890 5566 0.5795	18887 1179 18890 1428 0.1769 0.579	4 0.1084 2 0.1844 9 0.7664	1.1415 0.6720 1.1018 0.8362 0.3677 0.4432	0.0896 1.00 0.1826 0.87 0.5650 0.00	63 0.6813 24 0.8612 32 0.4515	0.1999 0.5889 0.2999 1.0089 0.9999 0.2711	0.7919	0.6255 0.66 0.2583 0.86 0.6573 -0.56	179 0.7972 1 165 0.9006 1 166 0.5007	15086 13252 13486 12259 13696 A1285	1329 03 1329 03	2900 1.2978 1.10 2558 1.3290 1.3 2739 0.7796 0.6	096 0.2658 794 0.3858 366 0.7987	0.8851 0.5 1.3139 1.3 0.1736 0.5	577 0.3368 547 0.2794 792 0.9120	0.7608 0.9057 1.0284 1.3275 -0.1729 0.5764	0.4160 021 0.4022 130 0.4140 0.21	14 0.8097 60 1.2196 98 0.5396	0.7961 0 0.2662 1 0.6669 -0	1265 0.8229 0.8778 2175 1.2285 0.8217 2151 0.5157 0.4834
MLA-R*15:01	0.7181 1.6081	0.5909 0.21 1.0911 0.12	62 0.7119 00 1.2662	06117 024 10692 024	0.7102 129 0.7577	0.5271 0.1779 0.7706 0.3255	0.6065 0.5254 0.5275 0.7785	0.2579	13927 0.6609 12106 1.0206	0.5526 0.2697 0.8966 -0.0268	0.6748 0.7113 1.0710 0.9808	0.5086 0 0.7611 1	6106 0.4085 2527 0.5485	0.6167 0.629 0.6905 1.332	8 0.4900 9 0.7129	0.8729 0.6955 0.8187 0.7484	0.680 0.20 0.6702 0.08	25 0.4996 58 0.7566	0.6840 -0.0663 0.9098 0.1416	0.5942 0.8651	0.9013 -0.243 0.8771 -0.154	21 0.5439 48 0.9107	1,6562 0.2666 1,8679 -0.1004	86942 61 12790 69	7286 0.2133 0.70 9365 0.3067 1.20	055 0.7626 861 0.8112	0.4925 0.5 -0.8139 0.6	660 0.3842 674 0.7111	0.3295 0.5749 -0.613 0.8556	0.5665 0.00 0.6760 -0.60	29 0.5798 (72 1.0418	0.9547 -0 0.5600 -0	0997 0.5827 0.9648 8106 1.0582 0.6615
MLA-R*227 MLA-R*27	0.808 -0.806 -0.775	0.9711 0.36 0.9711 0.46	99 12451 61 -03934 99 -03404	10633 0.26 0.9838 0.31 1,0168 0.35	26 0.596 26 0.596 30 0.599	0.5705 0.3258 0.6542 0.4009 0.6770 0.3996	0.5270 0.7796 0.5459 0.6568 0.5787 0.6787	0.4066	12129 1.0202 17254 0.7011	0.0021 0.2962 -0.7667 0.2903 -0.7600	1.0308 0.9829 0.7902 0.2748 0.7782 0.3029	0.7621 1 -0.0054 0 0.1227 0	2531 0.5421 8739 0.9951 8247 0.9903	0.8909 1333 -0.1600 0398 -0.0949 0346	9 0.7122 9 0.8727	0.1209 0.7484 0.7472 0.6180 0.7676 0.6676	0.6681 0.08 0.2979 0.76 0.3909 0.77	80 0.7566 15 0.6968 90 0.6540	0.9076 0.1462 0.2317 -1.1297 0.3329 -1.1564	0.9550	0.8748 -0.55 0.0829 -1.23 0.0946 -1.23	20 0.9106 92 0.6535 95 0.6799	1000 -0000 1000 -0000 1000 -0000	12796 05 10758 05	9977 -0.308 1.2 9319 -0.148 1.0 9017 -0.007 1.1	906 0.8944 222 0.9609	-0.8196 0.8 1.2964 0.3 1.3964 0.3	178 0.7118 551 0.0860	-0.6108 0.8555 1.2892 0.7608 1.2723 0.7729	0.6753 -0.60 0.0956 -0.30 0.1015 -0.40	66 1.0436 68 0.6791 66 0.7039	0.5617 -0 0.0618 -1 0.0659 -1	80% 1.0531 0.6631 6688 0.6897 0.0332 6653 0.7159 0.0357
ALA-2*25 ALA-2*25.00	2.1954 2.4090	0.7978 0.00 0.8575 0.00	53 20585 50 22695	0.7954 0.00 0.8600 0.00	0.2668 0.9961	0.5900 0.6536 0.6888 0.1489	0.1119 0.5972 0.8969 0.6977	0.8511	1997 0.6926 6627 0.8335	1.0665 1.0687 1.5997	0.7106 0.1836 0.8558 0.0720	2.5542 0 3.5923 1	9996 0.0106 3125 0.0062	2.6721 1.020 3.5888 1.359	2 0.0154 1 0.0089	0.29% 0.5720 0.5359 0.6683	0.6051 0.03 0.4092 0.29	16 0.5837 11 0.6749	0.8989 0.8416 0.6690 0.6074	0.5885 0.6688	0.8600 0.860	97 0.5936 36 0.6815	1.7509 1.3097 1.6979 1.4249	12000 0.1 11898 0.2	2755 1.2008 1.2 2811 1.8151 1.2	116 0.3218 052 0.2752	1.2576 0.5 2.0080 1.1	056 0.1649 724 0.0868	1.0276 0.9155 1.7547 1.1744	0.2617 1.34 0.1851 1.51	03 0.7790 27 0.8700	0.0809 1	2108 0.7778 0.1186 3972 0.8720 0.1091
MLA-0*37 MLA-0*37:01	-0.7376 -0.7370 0.0096	0.7629 0.30 0.7628 0.30 0.7929 0.90	81 -0.2821 83 -0.2817 13 -0.7866	0.8051 0.72 0.8051 0.72 0.8053 0.72	50 -0.3084 50 -0.3085 110 0.5000	0.6221 0.6200 0.6221 0.6200 0.7720 0.5160	0.2499 0.6488 0.2439 0.6488 0.2450 0.7850	0.7099	1191 0.8912 1186 0.8911	0.2092 -0.6696 0.2096 -0.6598	0.9178 0.4716 0.9176 0.4721 0.7093 0.3957	-13665 0 -13690 0	7995 0.0957 7995 0.0958 8011 0.5959	-0.9568 0.926 -0.9562 0.926 0.1964 0.915	3 0.2457 3 0.2460 7 0.9097	-1.4091 0.5999 -1.4099 0.5999 0.4499 0.5919	0.0577 -0.85 0.0579 -0.85 0.6677 0.16	80 0.6114 PR 0.6114 NO 0.6116	0.1809 -0.1765 0.1810 -0.1763 0.0163 2.0000	0.6622 0.6621 0.6666	0.7859 0.357 0.7860 0.357 0.0015 1.860	50 0.6665 52 0.6665 60 0.6777	15968 -2.2062 15961 -2.2068 10065 0.0627	09173 0.0 09173 0.0 1,0223 0.0	0162 -1.9986 0.9 0162 -1.9982 0.9 9659 0.175 1.0	518 0.0957 518 0.0958 301 0.9670	-1.4289 0.6 -1.4288 0.6 0.1210 0.6	332 0.0040 332 0.0041	-0.8736 0.6537 -0.8734 0.6537 -0.1623 0.6655	0.1815 -0.05	155 0.6790 109 0.6790 109 0.7166	0.8995 0	3508 0.7006 0.6170 3514 0.7006 0.6165 0162 0.7214 0.9277
ALA-810000 ALA-8100000	0.4242	0.7215 0.50 0.7232 0.60	66 0.3000 06 0.6185	0.7429 0.68 0.7662 0.57	00 -0.0568 100 0.2658	0.5778 0.9217 0.6088 0.6624	0.6094 0.5940 0.0929 0.6239	0.8968	19980 0.7512 17258 0.7962	0.1840 -1.8575 0.8546 -1.0984	0.7698 0.0778 0.8010 0.1722	0.6125 0 1.1277 0	8149 0.4520 8711 0.1955	0.5180 0.854 1.0587 0.908	5 0.5289 6 0.2439	0.0998 0.5602 0.0349 0.5969	0.8586 -0.47 0.9532 -0.86	82 0.5731 85 0.6082	0.4040 -0.6302 0.5666 -0.2930	0.6013	0.3258 -0.96 0.6620 -0.68	06 04535 50 04665	1.5627 2.9386 1.9522 8.6183	1.8572 0.1 20.5072 0.6	1136 2.0157 1.8 6763 8.6508 20.8	771 0.1081 090 0.6701	0.0541 0.3 0.0998 0.3	054 0.9289 152 0.8890	-0.3621 0.7180 -0.3072 0.7909	0.6997 -0.21 0.6749 -0.50	0.6697 (70 0.7186	0.7272 -0 0.8856 -0	6690 0.6805 0.5150 3689 0.7816 0.6836
ALA-8100 ALA-810000	-0.1865 0.0439	0.9954 0.60 0.4869 0.50	75 -0.2995 79 -0.0645	0.0068 0.32 0.0939 0.89	0.3904 60 0.4200	0.3383 0.2486 0.4009 0.2948	0.2244 0.8458 0.2571 0.4071	0.5257	13974 0.3609 15595 0.4563	0.2709 0.2060 0.1789 0.2799	0.8710 0.5797 0.4259 0.8781	-0.8537 0 -1.0207 0	9979 0.0057 6861 0.0058	-1.1994 0.618 -1.2199 0.509	5 0.0042 0 0.0158	0.2756 0.1092 0.2997 0.1708	0.9729 0.06 0.6966 0.10	18 0.3167 80 0.3772	0.8379 0.0873 0.7849 0.0902	0.3186	0.7841 -0.50 0.8853 -0.55	00 0.3271 61 0.3797	1.7552 -0.6561 1.6829 -0.3660	0.6685 0.1 0.5694 0.4	1619 0.8768 0.40 6978 0.4875 0.50	883 0.0732 804 0.4009	0.2792 0.9 -0.0988 0.4	594 0.4675 227 0.9666	0.0951 0.3695 -0.2296 0.4811	0.8834 0.31 0.5959 0.31	65 0.3455 69 0.3965	0.6506 0 0.3217 0	0081 0.3525 0.9817 2685 0.6061 0.5085
MEA-R*SO	-774.3209 0.2256	1029.1792 0.40 1.3099 0.80	18 -772.4049 12 12045	988.6552 0.43 1.3634 0.37	166 -6.5345 70 -0.0922	8.9152 0.6636 1.3634 0.9653	6.6001 9.6632 0.5222 1.8582	0.50%	17609 1.60% .9698 21.3270	0.6951 1.4812 0.5749 12.4769 :	1.5964 0.3529 21.4588 0.5609	-12379 1 -02791 1	3488 0.3587 2134 0.8219	-0.6643 1.396 0.5648 1.258	4 0.6342 5 0.6536	-1.0624 1.8884 0.4948 1.6691	0.4256 -0.57 0.7968 1.19	k1 1.9494 25 1.4714	0.6669 5.7606 0.4349 1.3022	12.4179	0.6427 6.427 0.3430 1.690	53 125322 06 12888	1.6082 -357.6204 1.1888 -1.4080	1115.9468 0.1 1.2701 0.1	7486 -395.2113 1122.2 2676 -1.0598 1.ir	534 0.7247 180 0.4218	-13640 13 1381 15	982 0.3902 987 0.5618	-0.8104 1.3092 1.3990 1.9907	0.5166 5.96 0.3710 1.80	92 18.1199 12 1.3798	0.7812 6 0.1917 2	6116 18.6927 0.7227 1988 1.3829 0.1197
ALA-2*50:01 ALA-2*51 MARA-2*51:01	0.23% -0.4562 -0.4563	1.3238 0.85 0.9231 0.66 0.9297 0.61	69 12367 20 -07171 05 -07307	13770 036 03919 046 03473 044	85 -0.1544 136 0.9958 95 0.9955	1.3783 0.9108 0.9113 0.2760 0.9147 0.7860	0.6664 1.9924 0.7997 0.9127 0.7984 0.9969	0.7976 S 0.4059 -	12802 21.4470 14085 1.0383	0.55669 12.7983 1 0.5579 -0.6820	21.5399 0.5531 1.0328 0.5096 1.0545 0.5143	-0.3202 1 1.2542 0 1.2574 0	2345 0.7956 8998 0.1621 8150 0.1624	0.5291 1.279 0.9090 0.927 0.9066 0.947	5 0.6792 0 0.3268 2 0.3268	0.4831 1.4826 0.4183 0.8083 0.4436 0.9204	0.7665 1.16 0.6068 0.18 0.5869 0.10	52 1.4851 23 0.8158 27 0.6400	0.4406 1.1999 0.8230 -0.3619 0.9060 -0.1957	1.2865 0.8212 0.8477	03530 169	61 1.3039 35 0.8271	1.1967 -1.5002 1.6609 0.9242 1.6539 0.9347	12991 0.1 10442 0.1 10589 0.1	2682 -1.1687 1.0 3761 0.7676 1.0 2764 0.7630 1.0	666 0.3936 306 0.4850 959 0.4990	1.1629 2.0 1.6998 1.1 1.6699 1.1	506 0.5680 789 0.168 997 0.169	1.7797 1.9879 1.3508 1.1856 1.3628 1.3058	0.3722 1.80 0.2545 0.60 0.7515 0.60	83 1.3928 83 0.9745 35 1.0141	0.1962 2 0.5158 0 0.5159 0	1702 1.6011 0.1214 8931 0.9754 0.6132 5180 1.0149 0.6064
ALA-2*55:01 ALA-2*57	-1.7625 -0.1650	1.2726 0.36 0.4092 0.75	65 -1.9795 32 0.6934	1.2945 0.12 0.5015 0.32	50 -1.0079 52 -0.4690	0.7962 0.1926 0.3636 0.2102	-1.2927 0.9127 0.2697 0.6239	0.1165	12895 0.8627 1515 0.6068	0.7972 -0.6120 0.0066 -0.9107	0.8761 0.6848 0.4769 0.0662	-1.8799 1 -0.2194 0	0506 0.0797 0908 0.5760	-2.1871 1.070 0.3928 0.679	9 0.0511	0.8005 0.7911 0.2698 0.8202	0.8056 -1.16 0.6006 0.68	19 0.7914 36 0.8911	0.1895 0.0995 0.0918 -1.1106	0.8827 0.8614	0.9109 -0.212 0.0011 -0.89	27 0.8879 82 0.6081	1.8106 -2.7929 1.0353 0.2148	1.8550 0.0 0.4940 0.4	0399 -2.1068 1.2 6637 0.7110 0.5	715 0.0236 964 0.2332	-0.8935 0.8 -0.3371 0.3	905 0.3502 901 0.3752	-1.1748 0.8922 0.4831 0.4476	0.1879 0.61 0.2800 0.91	50 1.0949 80 0.3635	0.5256 0 0.0091 -0	4360 1.0985 0.6982 7544 0.6844 0.0824
MLA-C*01:02 MLA-C*01:02	-0.3629 -1.2310 -1.7951	0.4246 0.56 1.1708 0.26 1.1806 0.16	58 0.3894 35 -0.9998 05 -2.1928	0.5215 0.45 1.2124 0.40 1.1965 0.06	52 -0.6698 96 2.7204 67 -1.0181	0.3595 0.1912 1.2221 0.0261 0.7571 0.1787	0.2872 0.6617 2.8887 1.2261 4.7380 0.7587	0.5256	2816 0.4180 3670 1.3755	0.0022 -1.0%4 0.3208 1.2828 0.3208 -1.8613	0.4985 0.0010 13652 0.3676 1,0074 0.1766	-0.2858 0 -0.2131 1 -0.0223	9962 0.6708 5605 0.8376 5996 0.3049	0.3654 0.688 0.0821 1.071 -1.3179 1.068	5 0.6596 7 0.9389 9 0.7356	0.8390 0.8251 1.9280 1.1687 0.0001 0.6001	0.2971 0.65 0.0997 1.98 0.5099 0.50	12 0.4022 28 1.1702 36 0.6996	0.1056 -1.0361 0.0902 0.3082 0.4315 -1.9009	0.8656	0.0036 0.72 0.7635 0.26 0.0063 -3.01	52 0.4186 14 0.9538	1.0000 0.1477 1.0002 -0.9155 1.0003 0.4657	0.4970 0.1 1.2233 0.4	7666 0.6760 0.6 6542 0.7252 1.2 7519 0.1934 1.4	084 0.2665 369 0.5577 363 0.9990	-0.4476 0.3 0.7124 1.0 1.4594 1.0	822 0.3415 918 0.4897 096 0.1563	0.4151 0.4574 0.7590 1.0671 1.7553 1.0096	0.860 4.90 0.6721 4.36 0.7168 -3.71	60 0.3678 66 0.9268 90 0.9990	0.0140 -0 0.6768 -0 0.0170 -3	6807 0.6650 0.1361 6929 0.9270 0.5989 9654 0.9069 0.0081
MLA-C*032	0.4238 0.5387	0.6399 0.30 0.6295 0.30	87 0.3433 18 0.3938	0.4490 0.44 0.6400 0.53	0.1483 66 0.1123	0.3543 0.6756 0.5176 0.8283	0.0675 0.1652 0.0417 0.5265	0.8586	10856 0.4157 11780 0.5772	0.9127 -0.2778 0.7578 -0.8256	0.4280 0.5169 0.5856 0.5792	-0.0705 0 -0.2409 0	6660 0.8765 6688 0.7085	-0.2511 0.867 -0.5035 0.662	9 0.5950 9 0.4475	0.0356 0.2998 0.1650 0.4972	0.9966 -0.19 0.7600 -0.02	0.8692 09 0.5058	0.8740 0.1858 0.8675 0.2309	0.8688 0.5212	0.7090 -0.09 0.6186 -0.06	62 0.3739 69 0.5269	1.7991 0.0972 1.9020 -0.0677	0.5399 0.6 0.7911 0.6	9571 0.0364 0.51 9309 0.1885 0.71	995 0.9682 972 0.8583	-0.2649 0.5 -0.8179 0.5	888 0.4957 508 0.5638	-0.5254 0.4010 -0.5005 0.5635	0.3900 0.30 0.3745 0.50	0.2969 80 0.5864	0.6083 0	0207 0.4064 0.9584 3662 0.5908 0.5850
MACCOST	0.3814 1.2809 1.7807	0.5889 0.51 0.5890 0.01	72 0.3474 94 1.1165 64 1.1163	1.00 1.00	0.3893 75 0.3879 75 0.3879	0.5181 0.6526 0.6629 0.6021 0.6621 0.6002	0.1889 0.5808 0.1647 0.4720 0.1665 0.4721	6.000	11529 0.6130 12019 0.5366 10019 0.5366	0.9018 -0.1900 0.0920 1.0995	0.0186	0.3321 0 1.9256 0 1.9256 0	6135 0.5983 6929 0.0055 6939 0.0055	1 1 2 2 2 2 2 2 2 2	6 0.6996 2 0.0127 2 0.0127	0.0689 0.4824 0.1024 0.4816 0.1029 0.4816	0.8966 -0.32 0.8126 -0.19 0.9117 -0.19	64 0.4912 38 0.4426 32 0.4427	0.4630 0.0295 0.6660 -0.0393 0.6670 -0.0393	0.5952 0.4872 0.4872	0.9560 -0.27 0.8710 -0.28 0.8710 -0.28	57 0.5472 1 47 0.6965 1	0.3362 0.5686 0.5382 0.5686 0.5382	0.7484 0.4 0.7519 0.4	6531 0.1095 0.74 6762 0.1972 0.7 6769 0.1977 0.7	Section 1	0.0520 0.5 1.2192 0.6	869 0.9249 289 0.0537	-0.2210 0.5565 0.9456 0.6279 0.6473 0.6279	100 100	98 0.5961 779 0.6066 90 0.6066	0.9595 -0 0.2305 0 0.3305 0	2753 0.5962 0.6462 5859 0.6093 0.3363 5860 0.6093 0.3363
ALA-C*05 ALA-C*05:00	-0.0558 -0.0720	0.4798 0.90 0.4761 0.80	69 -0.1954 15 -0.1515	0.6866 0.77 0.6868 0.75	986 0.4650 566 0.4685	0.4023 0.2790 0.4012 0.2660	0.2669 0.6098 0.2788 0.6102	0.5175	13753 0.4272 13858 0.4285	0.3296 0.3226 0.3679 0.3138	0.4357 0.6019 0.4370 0.6247	-0.7644 0 -0.7502 0	8948 0.1220 8964 0.1307	-0.9047 0.510 -0.8905 0.512	8 0.0762 6 0.0923	0.5911 0.9911 0.5867 0.9918	0.1907 0.40 0.1949 0.40	81 0.8979 61 0.8986	0.3096 0.2186 0.3096 0.2182	0.8765	0.5620 0.05 0.5722 0.00	29 0.3866 1 90 0.3856	1.8985 -0.3393 1.8988 -0.3178	0.5950 0.5 0.5928 0.5	1	990 0.4910 023 0.5176	0.0778 0.4 0.0718 0.4	954 0.8583 961 0.8692		0.7505 0.51 0.7616 0.50	0.6072 173 0.6081	0.2097 0 0.2139 0	3981 0.6160 0.3369 3967 0.6169 0.3616
MLA-C*05:02 MLA-C*027	-0.8325 0.0546 0.3009	0.3752 0.05	65 N/A N/A 36 -0.2660 97 -0.1064	0.3479 0.44 0.4210 0.79	-1.0261 02 0.0406 60 0.1003	0.3171 0.0012 0.2729 0.8817 0.3377 0.7589	N/A N/A N 0.3054 0.2949 0.4947 0.3527	0.8000 0.1664	18542 0.3603 12887 0.3508	0.00221 N/A N/A 0.5226 -0.5215	N/A 0.3359 0.1136 0.4990 0.5569	-0.9007 0 0.0649 0	2776 0.0130N) 2408 0.8487 2266 0.6485	-0.2291 0.368 -0.7699 0.465	N/A 0.5344	-1.1982 0.290F 0.0546 0.2562 0.0000 0.0000	0.0000N/A 0.8904 -0.88 0.9921 -0.44	N/O N/O N/O 05 0.2760	0.1680 0.0009 0.1736 0.0073	0.2966	0.0018 N/A 0.9972 -0.33 0.9911 -0.31	N/A N/A 56 0.2926 1 28 0.2679	-0.5041 0.0712 0.0712	0.4653 0.1 0.4254 0.6 0.5436 0.6	2576 N/A N/A N/A 8658 - 0.0764 - 0.6 9727 - 0.0969 - 0.5	N/X 895 0.8650 717 0.9617	-1.1986 0.3 -0.0747 0.3	666 0.0005 N/I 090 0.9053 507 0.7697	-0.5974 0.3930 -0.5974 0.3930		62 0.3196 55 0.2978 76 0.3971	0.0290 N/A 0.6990 -0 0.2120 0	N/A N/A N/A 0106 0.8197 0.9725 1472 0.4071 0.7759
HLA-C*07:02 HLA-C*07:08	0.3126 -2.3720	0.4711 0.60 1.3685 0.00	18 0.0912 21 -2.5154	0.6795 0.86 1.2992 0.05	02971 18 11795	0.6219 0.6816 1.2154 0.8868	0.1686 0.6906 0.7987 1.2160	0.6952 0.5306 -1247	12210 0.4848 19902 584170.5817	0.6685 -0.3825 0.9830 -12627.0193 5684	0.4870 0.4615 97.6228 0.9828	0.3353 0 -1.3436 1	5186 0.5180 0555 0.2030	0.1646 0.529 -1.5198 1.088	0 0.7557	0.1665 0.9954 0.5474 0.9170	0.6706 -0.08 0.5505 0.08	k1 0.3978 99 0.9901	0.9930 0.2009 0.9670 -13126.1018	0.8985	0.6153 0.00 0.6767 -13285.30	15 0.60% 108 466653.5697	19188 0.4610 19768 -1.1875	0.6766 0.6 1.1086 0.3	4758 0.8749 0.67 2923 -1.2586 1.12	791 0.5808 362 0.2629	0.1278 0.5 0.5528 1.3	072 0.6011 966 0.6696	-0.0278 0.5159 0.1272 1.9212	0.9569 -0.05 0.9233 -0.31	66 0.4499 69 1.0081	0.9550 -0 0.7527 -0	1509 0.6527 0.7888 5128 10101 0.6120
HLA-C*08:02 HLA-C*12	-0.1346 1.0944	0.8665 0.81 0.7952 0.15	65 -02967 57 -02855 66 03052	0.897 0.92 0.9897 0.92 0.7592 0.22	29 -0.6885 96 0.8656	0.7180 0.5184 0.7182 0.6964 0.5584 0.1818	0.5000 0.7281 0.6084 0.7289 0.5226 0.5762	0.405k 0.8627	14121 0.9841 14121 0.60%	0.6754 -0.5087 0.0059 1.8807	0.9942 0.6051 0.6248 0.0271	281.3853 495 0.9520 0	2105 0.5790 2105 0.5790 7395 0.1977	75.8622 197.970 215.9621 692.068 0.7969 0.759	0 0.7082 1 0.6607 6 0.3285	1.0988 0.6902 1.0988 0.5228	0.1046 0.92 0.1114 0.92 0.0445 0.70	18 0.6994 18 0.5370	0.1875 0.7688 0.1915 2.0186	0.7727	0.3229 0.617 0.0005 1.76	56 0.7779 148 0.5965	1.4288 9.6697 1.0094 -0.0927	23.9018 0.1 23.7911 0.1 0.8381 0.5	7620 8.0608 22.66 7972 8.8608 33.45 9689 0.2183 0.8	667 0.7927 654 0.7911 497 0.7979	0.8274 0.5 0.8299 0.6	018 0.8946 006 0.8687 887 0.1957	0.6363 0.9963 0.6714 0.6629	0.6716 026 0.6716 036	25 0.8967 02 0.6698	0.752 0 0.7500 0 0.262 0	1905 0.8945 0.8840 4533 0.6818 0.5061
MLA-C*12:03 MLA-C*15	1.9766 0.6198	0.7728 0.00 1.0515 0.50	69 1.1924 56 0.3992	0.7891 0.18 1.0625 0.70	0.5929 (7) 0.7025	0.6070 0.8352 0.9076 0.6376	0.2769 0.6226 0.6530 0.9285	0.6588	.4835 0.6368 12362 1.2351	0.0098 1.1819 0.8588 0.2168	0.6529 0.0709 1.2379 0.8625	0.9293 0 1.2697 1	7682 0.2167 0290 0.2176	0.6994 0.761 0.9279 1.049	7 0.3585 9 0.3761	0.8674 0.5390 0.1354 0.9169	0.10% 0.52 0.8826 0.06	60 0.5592 09 0.9271	0.8417 1,8779 0.9476 0.1910	0.5850 1.3617	0.0019 1.60: 0.8690 0.160	120 0.6036 69 1.1740	1.0079 -0.0859 1.8870 0.3361	0.8399 0.5 1.1408 0.7	9185 0.2767 0.8 7682 0.1886 1.17	509 0.7650 566 0.8706	0.7994 0.6 0.8842 1.0	609 0.3129 648 0.7157	0.4655 0.6489 0.2760 1.0538	0.6793 0.69 0.7936 -0.09	114 0.6790 152 1.1668	0.9517 0 0.9618 -0	3925 0.6890 0.5689 1076 1.1682 0.9268
MLA-C*15:00 MLA-C*16:01	-0.8560 -0.8667	0.8160 0.31 0.8165 0.26	79 -11533 08 -12053	0.8491 0.17 0.8490 0.15	10 -0.1889 10 0.2672 40 0.6268	0.8696 0.7516 0.8699 0.6696	0.1665 0.8541 0.5666 0.8741	0.8656 0.5368	.0009 1.2815 .7182 1.2896	0.1980 -2.0002 0.1980 -2.0002 0.1907 -1.8988	1.9009 0.1209 1.9009 0.1576	-0.3809 0 -0.8796 0	905 0.5856 6965 0.6977	-0.7286 0.706 -0.8209 0.716	8 0.3024 2 0.2504	0.8429 0.7279 1.0348 0.7561	0.2669 0.68 0.1712 0.90	72 1.8089 80 0.7947 83 0.7681	0.8518 0.6421 0.2338 0.6231	0.6677 0.6551	0.3215 0.51 0.3415 0.52	05 0.6535 97 0.6606	1.4107 -0.1672 1.4107 -0.3218	0.8050 0.6 0.8237 0.6	9397 -0.1608 1.2 8355 -0.8355 0.8 6960 -0.6876 0.8	722 0.6997 158 0.6809 397 0.5588	1.1591 0.5 1.1664 0.5	729 0.8788 065 0.3109 549 0.1524	1.0175 0.9290 1.2178 0.9530	0.2794 0.17 0.2794 0.17 0.1940 0.00	68 1.000 63 0.6934 64 0.7099	0.9007 -0 0.9004 0 0.9928 -0	9882 1.0038 0.5152 0699 0.6975 0.9270 0988 0.7126 0.8953
HEA-GRASTOS HEA-GRASTOS GR	-0.3392 -0.3170	0.3584 0.36 0.3562 0.35	29 -0.0329 25 -0.2558	0.3692 0.27 0.3664 0.33	51 -0.1711 126 -0.2672	0.3194 0.5923 0.3169 0.3961	0.1985 0.8258 0.27% 0.8258	0.5418 0.8861	12888 0.3785 13602 0.3782	0.6656 -0.3256 0.3258 -0.3865	0.3857 0.3989 0.3811 0.3105	0.0991 0 0.0621 0	9690 0.8002 9630 0.8655	0.0068 0.362 -0.0060 0.365	2 0.9900 0 0.9975	0.0978 0.2985 0.2099 0.2953	0.76k1 -0.16 0.6771 -0.25	83 0.3027 14 0.2997	0.6025 -0.7554 0.6016 -0.7961	0.3829 0.3290	0.0155 -0.30 0.0155 -0.80	03 0356 00 0356	-0.2909 1.0123 -0.2919	0.6669 0.1 0.6676 0.1	5474 0.8765 0.6 5324 0.8753 0.6	791 0.4295 790 0.4333	-0.1929 0.3 -0.2731 0.3	572 0.5893 572 0.4465	-0.3172 0.3620 -0.2962 0.3609	05122 -0.10 0.6119 -0.10	42 0.3630 62 0.3577	0.6702 -0.	1896 0.3643 0.6028 2056 0.3587 0.5675
HEA-GPA1*02:00 HEA-GPA1*02:00 HEA-GPA1*02:02	0.3007 0.37% 0.3865	0.3583 0.36 0.3899 0.35 0.7967 0.61	17 0.6067 29 0.6638 28 0.8811	0.8092 0.26 0.8022 0.26 0.8096 0.63	29 0.5680 89 0.3129 05 -0.2617	0.3193 0.5988 0.3590 0.3825 0.6865 0.7022	0.1960 0.8252 0.8152 0.8646 0.1850 0.6975	0.5657	12996 0.1784 13278 0.4256 13655 0.7633	0.8266 0.8612 0.8268 0.6229 0.8518	0.8857 0.8976 0.4331 0.8849 0.7515 0.6897	-0.0935 0 -0.0742 0 0.0958 0	9629 0.2993 8069 0.2552 7295 0.9066	-0.0051 0.982 0.0285 0.628 0.1288 0.769	1 0.9994 2 0.9469 9 0.9667	0.0939 0.2984 0.6067 0.8871 0.7996 0.6858	0.7529 0.19 0.2276 0.45 0.2085 -0.71	0.3056 25 0.3423 28 0.6417	0.4000 0.7567 0.3860 0.4710 0.2660 1.8883	0.8829 0.8686 0.6812	0.001H 0.77 0.201H 0.511 0.001H 1.621	28 0.3500 1 26 0.3766 1 02 0.6926	1.0290 0.2797 1.1796 0.1549 1.0400 0.8658	0.6668 0.1 0.5171 0.1 0.9661 0.1	5491 0.87% 0.67 7646 0.2512 0.51 2592 0.9385 0.90	790 0.6908 294 0.6952 816 0.3990	0.1939 0.5 0.6171 0.4 -0.4538 0.6	578 0.5876 332 0.1546 567 0.4896	0.296 0.869 0.699 0.695 -0.899 0.662	0.5090 0.51 0.5390 0.31 0.5399 1.51	36 0.005 36 0.005 83 0.005	0.4400 -0 0.4400 1	1891 0.9648 0.6087 2778 0.6085 0.6965 5554 0.8098 0.0546
HEA-GPR1*02:01 HEA-GPR1*02	1,3168 -0.5366	0.6816 0.00 0.4670 0.10	42 1.1622 86 -0.6594	0.7047 0.09 0.6589 0.15	65 0.4103 69 -0.1056	0.5545 0.4599 0.2540 0.7655	0.2051 0.5681 0.1869 0.8586	0.7181 0.6021	15056 0.6660 10584 0.4231	0.4477 0.4429 0.8905 -0.1235	0.6740 0.5111 0.4290 0.7729	-0.0507 0 -0.0971 0	6726 0.9400 6425 0.9331	-0.1384 0.695 -0.0909 0.660	8 0.8427 6 0.8436	0.1952 0.5057 0.2618 0.3276	0.6995 -0.00 0.4242 -0.18	0.5545 17 0.3324	0.9979 1.0241 0.3479 -0.1092	0.5580	0.2666 0.96 0.7529 -0.190	63 0.5649 67 0.3689	0.6095 0.5769 0.3276	0.8806 0.6 0.5437 0.5	6419 0.9654 0.80 5468 0.9684 0.50	960 0.6696 970 0.5817	0.6480 0.6 -0.1158 0.8	602 0.3266 950 0.7708	0.4804 0.6647 -0.3113 0.3999	0.6699 0.61 0.5660 -0.61	62 0.6256 60 0.3726	0.2670 0 0.2180 -0	6121 0.6299 0.3312 5560 0.3754 0.1605
HEA-GPRITOR HEA-GPRITOR HEA-GPRITOR(II	0.5884 0.1179 0.3163	0.4771 0.31 0.2765 0.66 0.2703 0.31	75 -0.6699 75 0.1801 19 0.3879	0.8896 0.17 0.2817 0.52 0.2796 0.16	27 0.1250 38 0.125	0.3608 0.6828 0.2298 0.5986 0.2251 0.5410	0.2106 0.3666 0.2088 0.2361 0.2129 0.2286	0.8901	12007 0.4557 10080 0.2683 10985 0.2591	0.6597 -0.2728 0.9761 0.0685 0.7181 -0.0358	0.4610 0.5547 0.2792 0.8021 0.2625 0.8931	0.1993 0 0.1992 0	0.892 0.8929 2857 0.6259 2805 0.6195	0.0156 0.886 0.3682 0.296 0.3679 0.289	6 0.9765 5 0.6167 8 0.6099	0.0565 0.2168 0.0565 0.2168	0.3975 -0.88 0.7926 0.12 0.6019 -0.03	64 0,2167 83 0,2187 80 0,2165	0.5560 -0.1000 0.8560 -0.1000	0.3567	0.5960 -0.26 0.5993 -0.26 0.5983 -0.26	06 0.3567 06 0.2391 00 0.2321	13096 0.5652 13286 -0.2557 13250 0.0965	0.5951 0.5 0.3685 0.6 0.3399 0.5	3422 0.5965 0.60 6631 0.2798 0.31 9165 0.0268 0.30	096 0.3296 566 0.6901 679 0.9632	-0.0572 0.4 0.0067 0.3 -0.1782 0.3	026 0.8870 548 0.9790 504 0.4766	-0.3629 0.4070 0.1004 0.2597 -0.3069 0.2569	0.6990 -0.00 0.6990 -0.00	120 0.3830 100 0.2561 31 0.2517	0.9977 0 0.9977 0	5758 0.9698 0.1899 0721 0.2588 0.7902 0796 0.2596 0.7716
HLA-GPR1*0E-02 HLA-GPR1*0E-01	-0.6139 -0.7992	0.4867 0.30 0.9733 0.43	72 -0.61% 99 -0.61%	0.6969 0.19 0.9755 0.66	05 -0.0542 75 -0.0236	0.4108 0.8951 1.0412 0.9920	0.0318 0.4145 0.2909 1.0538	0.9989 0.7925	13236 0.4709 12766 1.0542	0.8919 0.8294 0.1929 -1.2392	0.4771 0.4900 1.0909 0.2536	-0.0797 0 -0.2939 0	5379 0.8822 8777 0.7377	-0.1295 0.550 0.0664 0.892	0 0.8152	0.5977 0.4179 0.6882 0.8577	0.1526 0.4226 0.43	66 0.4247 08 0.8678	0.1512 -0.1366 0.6096 0.4465	0.4578	0.7650 -0.19 0.5786 0.67	0.6531 99 0.8153	1.7721 -1.2606 1.4085 0.9723	0.6654 0.0 1.2554 0.4	0549 -1.9506 0.67 6386 1.1642 1.27	791 0.0668 562 0.3626	0.8262 0.5 -0.0228 0.5	362 0.1516 056 0.9806	0.8912 0.5841 0.2708 0.9169	0.1271 0.69 0.7677 0.39	04 05134 98 07895	0.3476 0 0.6269 0	8966 0.5143 0.3362 8903 0.7991 0.5395
MLA-GPRI*33 MLA-GPRI*33:01 MLA-GPRI*13:01	0.1830 0.1829 0.9954	1.0072 0.80 1.0072 0.80 1.1484 0.41	99 0,0055 00 0,0054 59 0,7808	10569 0.99 10569 0.99 11592 0.49	69 1.0964 69 1.0964 60 -0.5692	1.3284 0.4153 1.3284 0.4153 1.0921 0.5813	1.1298 1.8798 1.1298 1.8798 0.6585 1.0391	0.6156 0.6156 0.5268	17285 2.2360 17285 2.2360 18964 1.6212	0.2226 2.6621 0.2226 2.6621 0.5809 -1.0968	23897 03967 23897 03967 18676 03107	-0.7641 1 -0.7642 1 0.1797 1	0.6887 0.036 0.6886 0.549 0.8770	-0.9715 1.108 -0.9716 1.108 -0.1008 1.168	8 0.3792 8 0.3792 2 0.9313	2.6874 1.4326 2.6874 1.4326 0.7018 0.8414	0.0607 3.00 0.0607 3.00 0.4045 0.57	14295 14295 19 0.8886	0.0968 1.2362 0.0968 1.2362 0.5000 0.5583	1.5201 1.5201 0.9521	0.4168 1.22: 0.4168 1.22: 0.5612 0.552	15 1.5765 15 1.5765 29 0.9805	1.4379 0.4888 1.4379 0.4885 1.5729 156.8682 1	13851 0.1 13851 0.1 12394,7795 0.5	7261 0.3986 1.30 7263 0.3981 1.30 9899 154.2851 12566.2	870 0.7719 870 0.7741 219 0.9902	16.6127 54.9 16.6131 54.9 -1.0321 0.8	032 0.7905 015 0.7905 714 0.2968	22.2%6 64.6%6 22.2%0 64.6%6 -1.1643 0.8873	0.7305 61.25 0.7305 61.25 0.1890 -1.62	05 233.9200 05 233.9200 50 1.0083	0.7923 68 0.7923 68 0.1071 -1	5669 267.9000 0.7902 5669 267.9000 0.7902 6110 1.0132 0.1118
HLA-OPRI*IX HLA-OPRI*IX:01	1.6774 1.6774	0.9967 0.00 0.9967 0.00	19292 19 19292	0.9579 0.06 0.9579 0.06	0.8495	0.7907 0.2860 0.7907 0.2860	1.1059 0.7974 1.1059 0.7976	0.1665	19624 0.9990 19624 0.9990	1.1826 1.1826 1.1826	1.0179 0.3654 1.0179 0.3654	0.0853 0	8326 0.9186 8326 0.9186	0.3706 0.860 0.3706 0.860	5 0.6667 5 0.6667	0.1528 0.7528 0.1529 0.7528	0.8991 0.50 0.8990 0.50	0.7609 0.7610	0.4949 0.5809 0.4949 0.5806	0.8812 0.8812	0.5100 0.776 0.5099 0.776	97 0.8912 98 0.8913	1.3822 -0.9631 1.3821 -0.9631	09798 03 09798 03	3328 -0.8307 0.91 3328 -0.8307 0.91	902 0.4016 902 0.4016	0.2188 0.5 0.2186 0.5	629 0.8206 680 0.8206	0.5296 0.9712 0.5299 0.9713	0.5855 -0.00 0.5850 -0.00	138 1,3466 132 1,3469	0.9792 0 0.9792 0	1586 1.2587 0.8988 1588 1.2580 0.8989
HEA-OQAI 101 HEA-OQAI 101	0.4100 0.4126	0.3083 0.11 0.3089 0.21	65 0.3853 39 0.5159	03136 031 03976 039	50 -0.8751 50 0.6771 40 0.9491	0.2587 0.0089 0.3653 0.0090	0.5824 0.2680 0.8488 0.3686	0.0268 0.0218	14054 0.2991 14055 0.4257	0.1608 -0.5755 0.8024 -0.2592	0.2984 0.0538 0.4331 0.5695	0.2190 1 0.2819 0 0.9114 0	0.009 0.009 3144 0.3699 6739 0.0545	0.9112 1.068 0.9292 0.929 0.9884 0.489	5 0.6886 0 0.0420	0.2297 0.2364 0.5772 0.8316	0.3271 0.07 0.0017 0.47	68 0.3002 80 0.3967	0.7529 -0.1059 0.1549 0.2039	0.3699	0.6709 -0.269 0.5680 0.066	67 635.9951 97 0.2561 04 0.3662	12924 -0.1664 1.2924 0.2944	0.3871 0.1 0.6834 0.1	7054 0.208 0.40 2510 0.8390 0.60	0.60% 051 0.60% 964 0.290%	0.0825 0.3 0.6030 0.3	817 0.7696 935 0.1256	-0.0654 0.2898 0.5070 0.4006	0.8214 -0.01 0.8214 -0.01	56 0.2757 04 0.3932	0.840k -0 0.840k -0 0.2797 0	7965 652.0025 0.9790 1727 0.2906 0.5929 3868 0.3981 0.3983
HEA-OQAI TOT/OZ HEA-OQAI TOT/OZ	-0.0142 0.6134	0.3615 0.96 0.7919 0.40	87 -0.1343 20 0.5185	0.3714 0.71 0.7358 0.46	76 -0.0696 is2 0.9977	0.3280 0.8798 0.5203 0.0552	0.0909 0.8306 0.9385 0.5292	0.7994	16606 0.1804 1.0124 0.5308	0.0825 -0.7886 0.9968 -0.0867	0.3825 0.0535 0.5620 0.8729	0.0064 0 -0.5289 0	9912 0.9870 9925 0.4450	-0.1922 0.408 -0.6863 0.708	2 0.7092 6 0.3327	0.85% 0.29% 0.6211 0.6907	0.2965 0.2066 0.59	79 0.3034 65 0.4979	0.1152 -0.2675 0.2813 -0.4806	0.8228 0.6912	0.4133 -0.347 0.3279 -0.59	95 0.3262 68 0.5005	12866 -0.6759 12367 -0.5056	0.5050 0.5 0.7926 0.6	3460 0.5865 0.5 4930 0.5688 0.7	129 0.2545 518 0.4688	-0.4005 0.3 -0.0180 0.5	619 0.3685 852 0.9755	-0.5130 0.3668 -0.0967 0.5913	0.1619 -0.11 0.8700 -0.90	.79 0.3709 196 0.5212	0.7506 -0 0.0671 -1	1850 0.3791 0.6200 1009 0.5305 0.0380
HEA-DAN 10203 HEA-DAN 10203 HEA-DAN 10203	-0.1969 -0.3924	0.8597 0.66 1.0715 0.75	67 03880 89 -03428 12 -02181	0.808 0.60 0.8705 0.51 1.0985 0.86	21 -0.1150 55 -0.8902	0.2921 0.6938 1.0552 0.6042	0.1850 0.2967 0.7987 1.0676	0.5329	15252 0.8475 13509 1.2558	0.1907 0.4964 0.4979 0.8882	0.8527 0.1956 1.2853 0.4921	-0.1851 0 1.1676 1	2541 0.6012 1541 0.6012	-0.3211 0.079 -0.3617 0.362 1.3285 1.156	0 0.6697 6 0.2499	0.01% 0.2777 0.0261 0.8520	0.9660 -0.06	66 0.2976 27 0.2795 67 0.8651	0.8786 0.1429 0.9386 0.6090	0.3941	0.6270 0.09 0.5252 0.67	85 0.3165 13 0.2978 199 0.9700	1.7981 -0.6602 1.7882 1.4001	0.4152 0.1 1.3061 0.2	3071 0.7982 0.4: 1118 0.7905 0.4: 2769 1.4164 1.2:	365 0.0941 219 0.0834 981 0.2752	-0.3087 0.3 -0.3468 0.3 -0.7736 1.1	908 0.4455 802 0.5121	-0.3036 0.3234 -0.358 1.3846	0.8599 -0.50 0.3479 0.54 0.5345 0.20	03299 05 03239 85 03733	0.6487 0 0.8306 0	1226 0.9039 0.2156 1226 0.9278 0.7079 1684 0.9920 0.8679
HLA-DQA1*05:01 HLA-DQ81*02	0.0962	0.3763 0.50 0.3289 0.75	72 -0.3755 67 -0.0051	0.3994 0.34 0.3412 0.98	75 0.2612 95 0.065	0.3107 0.4005 0.2762 0.8676	0.0656 0.8296 0.0206 0.2991	0.8517	1.6060 0.3514 1.6318 0.3179	0.6055 0.1766 0.6195	0.1665 0.2685 0.1245 0.2966	0.1210 0 0.1277 0	2933 0.7586 2323 0.7008	-0.5607 0.625 0.0809 0.344	7 0.7031 1 0.8142	0.3384 0.2903 0.1524 0.2569	0.2636 -0.02 0.5530 0.06	86 0.3096 79 0.3603	0.9264 0.2916 0.7940 0.3179	0.3112	0.3497 0.06: 0.2613 0.27	13 0.3269 152 0.2866	1.8994 0.4003 1.3370 0.4917	0.4956 0.4 0.4126 0.2	4154 0.8842 0.5: 2884 0.5112 0.4:	962 0.5176 170 0.2202	0.6418 0.8 0.4802 0.8	566 0.0725 062 0.1169	0.3000 0.3799 0.3909 0.3060	0.6289 0.66 0.2021 -0.00	13 0.3430 62 0.3112	0.0499 0 0.9861 -0	5186 0.3579 0.1476 0645 0.9114 0.9358
ALA-DQ81*02:02 ALA-DQ81*02:02 ALA-DQ81*03	0.0181 0.0181 -0.4128	0.4227 0.96 0.4227 0.96 0.2962 0.36	58 0.1476 20 -0.3672	0.6968 0.79 0.8109 0.29	66 -0.5656	0.8628 0.6063 0.2645 0.0149	0.0287 0.879 0.0268 0.8758 0.6829 0.2504	0.9686 0.0568	13969 0.3921 10016 0.2705	0.8902 0.5720 0.9952 0.1554	0.4043 0.1571 0.2811 0.5804	0.1799 0 0.0476 0 -0.4274 0	0999 0.90% 2950 0.1476	0.5600 0.621 -0.3667 0.016	8 0.7000 8 0.2217	0.2298 0.1116 0.1457 0.2242	0.1180 0.08 0.4889 0.03 0.1291 -0.14	62 0.3634 82 0.3634 25 0.2319	0.913 0.38% 0.913 0.38% 0.538 -0.2290	0.3670	02519 060 03371 -006	77 0.6236 70 0.3566 84 0.2666	1.0866 0.5575 1.2900 -0.3672	05105 0.1 03994 0.1	2768 0.6990 0.5: 2812 0.890 0.8:	0.99 0.36971 175 0.2569 777 0.3055	0.925 0.3 -0.9918 0.3	868 0.8109 645 0.195	0.8851 0.4033 0.8861 0.4033 -0.2019 0.2735	0.8380 -0.30 0.8606 -0.00	69 0.3779 69 0.3779 68 0.2639	0.4182 -0 0.9117 0	1909 0.9844 0.6990 1252 0.2710 0.6441
ALA-0091102:02	-0.5369 0.4454	0.3729 0.56 0.5905 0.46	62 -0.7723 07 0.6123	0.3869 0.06 0.6127 0.31	0.0005 27 0.0005	0.5968 0.5676 0.4908 0.9991	0.9154 0.9029 0.0907 0.4945	0.2968	19276 0.3518 10887 0.5266	0.0086 0.8896 0.8657 -0.1192	0.3557 0.0169 0.5297 0.8908	-0.6883 0 0.3164 0	9696 0.1968 5438 0.5607	-0.7666 0.383 0.8847 0.565	8 0.0554 8 0.3878	0.0942 0.2777 0.1557 0.4175	0.7945 -0.29 0.7092 0.20	59 0.2851 87 0.4179	0.4090 0.3420 0.6158 -0.0876	0.2992 0.4675	0.4169 0.161 0.8549 -0.00	58 0.3038 97 0.4500	1.6856 -0.7123 1.9403 -0.0260	0.4972 0.1 0.6296 0.5	1092 0.9088 0.4 9667 0.0128 0.6	518 0.0654 355 0.9839	0.0965 0.3 -0.1611 0.4	945 0.9607 683 0.7908	-0.1905 0.3690 -0.1029 0.4729	0.7097 0.74 0.8295 -0.62	29 0.862 23 0.6965	0.0367 0 0.2119 -0	7101 0.3487 0.0417 5876 0.0987 0.2387
HLA-0091*00.02	0.3824	1.0715 0.72 1.0715 0.72	12 -02121 12 -02121	10935 0.86 10935 0.86	55 -0.7262 55 -0.7313	1.0503 0.4893 1.0508 0.4865	0.6312 1.0624 0.6365 1.0630	0.552e 0.5490	1.8509 1.2553 1.8509 1.2553	0.8979 0.8822 0.8979 0.8882	1.2853 0.4920 1.2853 0.4920	1.1676 1 1.1676 1	1338 0.3031 1338 0.3031	13085 1150 13085 1150	6 0.2699	0.0762 0.866	0.9258 -0.02 0.9280 -0.02	16 0.8567 27 0.8572	0.9775 0.6080 0.9789 0.6080	0.9693	0.5252 0.67 0.5252 0.67	729 0.9700 1 729 0.9700	1.6872 1.6201 1.6872 1.6201	13061 0.1	2769 1.4164 1.2 2769 1.4164 1.2	981 0.2752 981 0.2752	-0.8555 1.1 -0.8564 1.1	737 0.4665 763 0.4669	-0.8036 1.1792 -0.8028 1.1797	0.8952 0.20 0.8958 0.20	85 0.9733 85 0.9733	0.8300 0	5634 0.9920 0.9679 5634 0.9920 0.9679
ALA-DOST*05 ALA-DOST*05:01	0.5047 1.3065	0.999 0.17 0.494 0.00	96 0.5829 97 1.2421	0.9959 0.19	08 0.9218 29 1.1329	0.855 0.0095 0.4951 0.0096	0.8197 0.8587 1.0319 0.4386	0.0229	10987 0.4552 11446 0.5084	0.9258 -0.1115 0.7761 -0.2984	0.4224 0.7918 0.5165 0.5634	11429 0 17294 0	6658 0.0142 6709 0.0102	1.2233 0.477 1.7922 0.678	2 00104 5 00107	0.4998 0.8229 0.5902 0.8365	0.1209 0.89 0.1189 0.50	19 0.3270 29 0.3823	0.2908 0.2175 0.1889 -0.1518	0.8690 0.4008	0.5332 0.07:	18 0.3539 71 0.4108	1.8450 1.0289 1.4541 1.1146	0.0007 0.1	1227 1.0657 0.6 1519 1.1110 0.7	366 0.1152 809 0.1548	0.6600 0.3	915 0.0918 898 0.1167	0.5538 0.3979 0.6537 0.4920	0.1688 0.00	56 0.3848 86 0.4278	0.236H 0 0.730H 0	2727 0.3896 0.3275 0825 0.6320 0.8486
MLA-DQ82*06 MLA-DQ82*06:02	0.0694	0.3998 0.80 0.4264 0.30	83 -0.0914 82 0.3885	0.3476 0.92 0.4349 0.37	90 0.2700 127 -0.0005	0.2036 0.3508 0.3832 0.9969	0.2126 0.2976 0.0268 0.3876	0.4768	16006 0.1277 16815 0.4962	0.0668 -0.7288 0.1182 -0.7951	0.8382 0.0297 0.4386 0.0938	-0.3745 0 0.0494 0	3196 0.2827 6191 0.9122	-0.5500 0.367 -0.0776 0.869	5 0.1327 4 0.8671	0.0129 0.2704 0.6942 0.3479	0.8739 -0.17 0.1555 -0.58	04 0.2766 P1 0.8521	0.5349 -0.2954 0.0955 -0.5021	0.2903	0.3089 -0.42	169 0.2967 165 0.3830	1.5896 -0.7234 1.1257 -0.5684	0.4208 0.0 0.6032 0.0	0856 0.856 0.6 3661 0.6573 0.6	358 0.0523 074 0.2792	-0.1648 0.1 -0.6292 0.4	278 0.3658 590 0.1332	-0.4804 0.3333 -0.3066 0.4213	0.1695 -0.61 0.0935 -0.60	38 0.3285 38 0.4480	0.5672 -0.	5557 0.3127 0.0948 4551 0.4658 0.3078
ALA-0091*06:08 ALA-0091*06:08	0.5645 -1.0906	0.7015 0.42 1.2768 0.41	10 0.5095 96 -1.1706	0.7069 0.47 1.2997 0.36	113 0.7868 66 -0.2100	0.5212 0.1811 0.8762 0.8287	0.7438 0.5291 0.2675 0.9906	0.1998	12887 0.5606 15695 1.0600	0.5982 -0.4282 0.5829 -0.6482	0.5521 0.4633 1.0697 0.5601	-0.5791 0 -1.6950 1	6751 0.3958 0579 0.1150	-0.7217 0.693 -1.8945 1.121	1 0.2979 2 0.0928	0.4857 0.4679 0.6168 0.8055	0.3299 0.41 0.4254 0.52	53 0.5047 15 0.8127	0.4106 -0.6201 0.5210 0.4404	0.4979	02130 -0.721 0.6224 0.31	58 0.5076 IS 0.8998	1.5565 -0.5545 1.7109 -1.5679	0.7221 0.4 1.1405 0.1	6426 0.6060 0.7 1692 -1.602 1.1	977 0.4114 566 0.1561	0.011 0.5 0.0554 0.5	914 0.9668 976 0.9548	-0.0685 0.5968 -0.0722 0.5862	0.9952 -5.00 0.9456 0.20	05 0.5278 65 1.0029	0.0569 -1 0.7679 0	0972 0.5275 0.0412 2213 1.0064 0.9259
WEN-CHRILOTEDS WEN-CHRILOTEDS	1.5526 2.1095	0.6280 0.00 1.5271 0.36	28 1.6815 84 1.989	0.6660 0.00 1.5359 0.20	12983 100 47.9791	0.5636 0.0217 64.0642 0.2762	1.1811 0.5698 42.6779 46.2840	0.0800	L8129 0.6086 L8802 1.7939	0.6060 -0.6817 0.6237 0.7918	0.6188 0.6164 1.8290 0.6640	1,9979 0 1,8161 1	8984 0.0262 8084 0.1972	2.0997 0916 1.5952 1.408	4 00217 0 02668	0.4485 0.4710 2.6329 1.4361	0.8664 0.81 0.0667 2.48	k2 0.4781 66 1.4502	0.5057 -0.4856 0.0866 1.2382	0.4755 1.2948	0.3071 -0.69 0.3389 119	62 0.6871 62 1.3166	1.565 1.8586 1.3699 0.3286	1.6125 G: 1.8022 G:	1885 1.8762 1.4 9288 0.0298 1.8	278 0.1888 064 0.9821	0.2886 0.5 3.8057 1.5	787 0.6180 670 0.0518	0.1688 0.5845 3.5902 1.9512	0.8056 -0.26 0.8658 0.76	0.6975 63 1.2138	0.5606 -0 0.5397 0	4247 0.5053 0.6006 7226 1.2173 0.5528
ACT 120 ACT	0.0947		16 -0.2298 29 -0.2299	0.100 0.00	0.3465 03 0.3467	0.3659 0.3465 0.3659 0.3462	0.0965 0.3952 0.0982 0.3952	0.9216	13512 0.4611 13518 0.4611 15070 0.1665	0.4259 0.0234 0.4251 0.0245	1997 1998		6799 0.7300 6799 0.7309 3640 0.467	-0.1102 0.523 -0.1108 0.523	6 08330 6 08326	0.4401 0.3394 0.4408 0.3395	A	27 0.3628 28 0.3624 50 0.1896		0.3959	0.7098 -0.2% 0.7099 -0.2%	0.4188 03 0.4188	1	04099 04 04099 04		600 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0	0.7607 0.4 0.7607 0.4	256 0.0347 256 0.0347	0.8176 0.4611 0.8176 0.4611	0000 0000	96 0.6218 09 0.6218 68 0.219*	0.6798 0 0.6802 0	1999 1999
MLA-CHR1*0E-07 MLA-CHR1*0E-07	-0.3895 -0.895	0.4915 0.86 0.4915 0.86 1.4886 0.86	67 -0.3585 76 -0.3582	0.4423 0.41 1.5052 0.72	77 -0.2131 79 -0.2131 70 -0.3515	0.3607 0.5434 1.0059 0.7268	-0.1419 0.8026 -0.2882 0.8545 -0.5675 1.0075	0.5206 0.5788	1.8091 0.4195 1.2658 2.4334	0.0076 0.0025 0.1822 2.8724	0.6213 0.0683 2.3876 0.2289	-0.2581 0 -0.6668 0 0.6060 1	0.086 6141 0.1086 9630 0.6981	-282 0375 -04702 0423 03111, 1420	6 01128 6 09658	0.0011 0.918 0.0011 0.9186 0.6969 1.0007	0.9979 0.00 0.9979 -0.00 0.6962 -0.99	0.28% 6 0.9216 67 1.0271	0.9986 0.2948 0.3629 0.8958	0.3612 1.4188	0.6329 0.275 0.5279 -0.395	71 0.3458 94 1.4194	1.6222 -1.0764 1.3981 -0.4047	0.6799 0.0 1.6872 0.1	0.8787 0.40 0249 -1.0928 0.40 7855 0.7264 1.50	968 0.0261 229 0.6348	0.0991 0.1 -1.0940 1.3	679 0.8729 810 0.4106	0.0724 0.9722 -1.8101 1.8078	0.8458 0.00 0.8458 0.00	56 0.3768 22 1.6587	0.9827 0 0.2565 1	0682 0.8822 0.8680 4928 1.4718 0.8108
MLA-CRR1*07 MLA-CRR1*07:01	-0.2256 -0.2257	0.8305 0.46 0.8305 0.46	69 01926 68 01925	0.3835 0.72 0.3835 0.72	96 -0.7409 97 -0.7408	0.2831 0.0089 0.2831 0.0089	0.3959 0.3268 0.3958 0.3268	0.2250	13871 0.3116 13871 0.3116	0.2540 -0.0683 0.2545 -0.0683	0.3602 0.8606 0.3602 0.8606	-0.2604 0 -0.2604 0	1275 0.4266 1275 0.4266 1214 0.5171	0.1169 0.362 0.1150 0.362	6 03639 6 03637	0.5001 0.2548 0.5001 0.2548	0.0097 0.02	24 0.2984 25 0.2984 35 0.7969	0.9135 -0.3228 0.9136 -0.3228	0.3699	0.8090 0.170	94 0.3139 94 0.3139	1.5908 0.4078 1.5908 0.4074	0.6062 0.0 0.6062 0.0	2126 0.7956 0.4 2125 0.7957 0.4 4144 0.915	772 0.0956 774 0.0956 680 0.485	-0.1084 0.1 -0.1084 0.1	963 0.2965 963 0.2967 980 0.53**	0.2558 0.3699 0.2559 0.3699	0.6667 -0.56 0.6666 -0.56	077 0.2939 06 0.2939	0.0655 -0 0.0656 -0	4255 0.3406 0.2115 4254 0.3406 0.2116 1715 0.9806 0.2116
NEW-CHRILONGS NEW-CHRILONGS	-0.1653 -0.1653	1.1097 0.80 1.2978 0.90	58 0.1547 68 -0.3997	11953 0.89 13908 0.76	-1.085 -0.868 30 -0.987	1.0594 0.4117 1.2419 0.4255	0.7939 1.0710 -1.0398 1.2467	0.6662	1.6505 1.2993 1.7680 1.3430	0.6066 0.6908 0.5676 0.5570	1.8290 0.6082 1.8587 0.6807	1,0009 1 0,6037 1	0.5170 0.5170 0.5122	12161 1186 02278 1329	8 0.3055 0 0.8635	0.0184 0.8568 -1.7930 1.5064	0.9829 0.05 0.2971 -1.78	74 0.8699 R2 1.6914	0.9676 0.1969 0.2908 0.9958	1.0152 1.1285	0.8562 0.2K 0.8072 0.7K	027 1.0299 1 03 1.1982	1.7761 1.3362 1.5186 1.1007	13301 03 14661 04	2151 1.3490 1.8 4529 0.8050 1.4	290 0.3064 820 0.5889	-0.7976 1.1 -2.5337 1.5	862 0.5061 072 0.1860	-0.7535 1.1893 -2.5683 1.8723	0.5264 0.54 0.5785 0.55	0.8931 111 1.0049 129 1.1508	0.8883 0	1100 1.0121 0.9100 3709 1.1609 0.7500
MLA-CRR1*12:00	0.2028 0.7977	0.6925 0.76 0.5929 0.41	96 -0.6292 38 0.5398	0.7003 0.53 1.0602 0.60	00000 000 -0.1197	0.6418 0.9429 0.9623 0.8999	0.0307 0.6436 0.3573 0.9896	0.9620	1.6887 0.6012 1.5866 1.1138	0.4179 0.4437 0.1548 1.6367	0.6095 0.6666 1.1668 0.1535	0.3963 0 -0.5047 0	7611 0.5928 9697 0.6027	0.3652 0.751 -0.7229 1.009	2 0.8259 1 0.4720	0.3620 0.5801 0.8009 0.9015	0.5127 -0.40 0.7985 -0.61	17 0.5896 PR 0.9117	0.4956 0.1221 0.4861 -0.3176	0.5566	0.8263 0.056 0.6998 -0.341	06 0.5634 54 0.8411	1.9284 1.0056 1.6819 -0.0512	10258 0.0 15375 0.0	3269 0.8643 1.0 9725 0.3266 1.5	366 0.4035 364 0.9366	02187 03 01969 16	965 0.7717 900 0.9000	0.1271 0.3179 -0.1037 1.0906	0.8650 1.30 0.9243 0.34	0.6656 01 1.199	0.0502 I 0.7506 -0	2519 0.6698 0.0616 8077 1.1471 0.7228
WEN-CHR1,15:05 WEN-CHR1,15:00	0.7929 0.7929 -2.0697	0.7549 0.60 0.7549 0.30 0.9905 0.00	03422 05 07159 65 -23607	0.7578 0.34 0.7578 0.34 0.9354 0.05	0.2150 168 0.7178 16 -0.9920	0.5295 0.5625 0.5329 0.1821 0.2994 0.2123	0.5924 0.5464 -1.1489 0.8148	0.2051 0.1588	12342 0.5690 16688 0.9628	0.6697 -0.8581 0.6781 -0.8112	0.5607 0.5231 0.5620 0.3937	-0.7249 0 -0.7249 0 -1.3512 0	7085 0.3068 8782 0.3217	-0.8768 0.721 -0.8768 0.721 -1.5862 0.917	9 00127 5 02249 1 00837	0.390F 0.5024 0.0183 0.6678	0.508 0.16 0.686 0.92 0.9781 -0.18	60 0.5091 21 0.6740	0.5220 -0.7697 0.7870 0.4580	0.5069	0.1289 -0.875 0.6000 0.256	23 0.5159 88 0.8031	10909 -0.6060 13677 -1.3225	07457 04 10618 03	-1.12% 0.9 4164 -0.6712 0.7 2130 -1.4483 1.0	569 0.3752 754 0.1781	-0.0814 0.5 -0.1866 0.3	940 0.9444 945 0.8527	-0.0831 0.5990 -0.8321 0.7990	0.8896 -0.50 0.8896 -0.50	65 0.5348 111 0.8820	0.0292 -1 0.5995 0	0.0578 0.2267 2582 0.5400 0.0207 3871 0.8861 0.6615
MLA-CRR1*14 MLA-CRR1*14 MLA-CRR1*14	-1.3547 -1.4844	1	1				1999 1999	American American	1999 1999	1998 1998	0.9263 0.7238 0.9041 0.4717	-11996 0 -19961 1		1 1 1 1 1 1 1 1 1 1	1	1999 1999	April Apri	1	0.9590 1.8691 0.5890 1.5501		100 100	1	1.1800 -18068.2508 52 1.2366 -1866.2642 11	Section Sect	1	586 0.9800 475 0.9871		1	1 1 1 1 1 1 1 1 1 1	1	1		1991 1992
47 CM81,12 Q1 47 CM81,12	0.3279	0.4114 0.41 0.4175 0.41	02170 30 02604	0.4270 0.54 0.4270 0.54	0.2967	0.891 0.6138 0.3706 0.7927	0.0666 0.3755	0.8993	16296 0.6316	0.5806	0.4340 0.1147	0.1328 0 0.1328 0	0.0227 0.005 0.0009	0.0804 0.652 0.0804 0.655	* 0.9618	0.3554 0.3650	0.3215 -0.32 0.3066 -0.66	0.1096	0.1996 -0.3604	0.8797	0.341) 0.45	0.379	0.039 1.2551 -0.034	0.5994 0.6	4229 0.5686 0.60	0.8620	0.6124 0.6	0.1895 0.1293	-0.7099 0.4172 -0.7099 0.4190	0.0900 -0.21	0.4609 168 0.4661	0.5832 -0	2909 04672 0.5129