**Supplementary Material**

**Supplementary Table S1.** The reimbursement date and drug supply daysa of bDMARD and tofacitinib

|  |  |  |  |
| --- | --- | --- | --- |
| **Agent** | **Dosage (mg)** | **Drug supply (days)** | **Reimbursement start date in Taiwan** |
| Etanercept | 25 | 3.5 | 2003/3/1 |
| 50 | 7 | 2013/10/1 |
| Adalimumab | 40 | 14 | 2004/9/1 |
| Rituximab | 100 | 180 | 2008/11/1 |
| Golimumab | 50–100 | 28 | 2012/1/1 |
| Tocilizumab | 80, 200, 400 | 28 | 2012/5/1 |
| Abatacept | 250 | 7 | 2012/6/1 |
| 125 | 28 | 2015/8/1 |
| Tofacitinib | 5 | 0.5 | 2014/12/1 |
| 11 | 1 | 2018/6/1 |

Abbreviation: bDMARD, biologic disease-modifying antirheumatic drug.

a Drug supply days = Imputed days’ supply.

**Supplementary Table S2.** Cox proportional regression analysis of the cumulative probability of switching/discontinuation (for a maximum follow-up of 6 years)

|  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| Variable | **Univariate analysis** | | | |  | **Multivariate analysisa** | | | |
| cHR | 95% CI | | *P* value |  | aHR | 95% CI | | *P* value |
| **Index treatment** |  |  |  |  |  |  |  |  |  |
| Etanercept | 1.00 | (Ref.) | | |  | 1.00 | (Ref.) | | |
| Adalimumab | 1.16 | 1.07 | 1.26 | 0.0003 |  | 1.17 | 1.08 | 1.28 | 0.0001 |
| Golimumab | 0.87 | 0.78 | 0.96 | 0.0069 |  | 0.88 | 0.79 | 0.97 | 0.0131 |
| Tocilizumab | 0.53 | 0.46 | 0.62 | <.0001 |  | 0.52 | 0.44 | 0.61 | <.0001 |
| Abatacept | 0.65 | 0.57 | 0.73 | <.0001 |  | 0.62 | 0.55 | 0.71 | <.0001 |
| Tofacitinib | 0.71 | 0.6 | 0.84 | <.0001 |  | 0.71 | 0.60 | 0.85 | 0.0002 |
| **Index year** |  |  |  |  |  |  |  |  |  |
| <=2014 |  |  |  |  |  | 1.00 | (Ref.) | | |
| >=2015 |  |  |  |  |  | 1.04 | 0.96 | 1.13 | 0.3750 |
| **Age at index** |  |  |  |  |  |  |  |  |  |
| 18–29 years |  |  |  |  |  | 1.00 | (Ref.) | | |
| 30–39 years |  |  |  |  |  | 0.91 | 0.75 | 1.09 | 0.2956 |
| 40–49 years |  |  |  |  |  | 0.79 | 0.67 | 0.94 | 0.0081 |
| 50–59 years |  |  |  |  |  | 0.85 | 0.72 | 1.00 | 0.0449 |
| 60–69 years |  |  |  |  |  | 0.90 | 0.76 | 1.07 | 0.2274 |
| ≥70 years |  |  |  |  |  | 1.07 | 0.90 | 1.28 | 0.4590 |
| **Gender** |  |  |  |  |  |  |  |  |  |
| Female |  |  |  |  |  | 1.00 | (Ref.) | | |
| male |  |  |  |  |  | 1.01 | 0.93 | 1.10 | 0.8328 |
| **CCI** |  |  |  |  |  |  |  |  |  |
| CCI≤1 |  |  |  |  |  | 1.00 | (Ref.) | | |
| CCI=2 |  |  |  |  |  | 1.02 | 0.94 | 1.10 | 0.7263 |
| CCI≥3 |  |  |  |  |  | 1.03 | 0.93 | 1.14 | 0.6257 |
| **Comorbidities** |  |  |  |  |  |  |  |  |  |
| HBV |  |  |  |  |  | 0.90 | 0.74 | 1.10 | 0.2984 |
| HCV |  |  |  |  |  | 0.95 | 0.74 | 1.21 | 0.6607 |
| CKD |  |  |  |  |  | 1.18 | 0.92 | 1.51 | 0.1931 |
| COPD |  |  |  |  |  | 1.33 | 0.92 | 1.91 | 0.1275 |
| DM |  |  |  |  |  | 1.10 | 0.98 | 1.24 | 0.1125 |
| **Concomitant medications**b |  |  |  |  |  |  |  |  |  |
| Steroid |  |  |  |  |  | 1.35 | 1.21 | 1.51 | <.0001 |
| csDMARD, MTX |  |  |  |  |  | 0.83 | 0.76 | 0.91 | <.0001 |
| csDMARD, Non-MTXc |  |  |  |  |  | 1.18 | 1.05 | 1.34 | 0.0065 |

Abbreviation: aHR, adjusted hazard ratio; CCI, Charlson Comorbidity Index; cHR, crude hazard ratio; CI, confidence interval; CKD, chronic kidney disease; COPD, chronic obstructive pulmonary disease; csDMARD, conventional synthetic disease-modifying antirheumatic drugs; DM, diabetes mellitus; HBV, hepatitis B; HCV, hepatitis C; MTX, methotrexate; Ref., reference group.

aAdjusted for age at index, gender, CCI, and comorbidities, use of MTX, use of other csDMARDs other than MTX, and use of steroid.

bConcomitant medications is followed from index date to switching/discontinuation or end of data.

cHydroxychloroquine, leflunomide and sulfasalazine

**Supplementary Table S3.** Events occurred within 3 months prior to the date of switch or discontinuation

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
|  | Among patients who switched or discontinued their index biologic | | | Observation period | Definition of events |
| **Total** | **Switched** | **Discontinued** |
| **(N=3,464)** | **(N=1,479)** | **(N=1,985)** |
| Pregnancy | 74 (2.1%) | 22 (1.5%) | 52 (2.6%) | Within 3  months (90  days) prior to  the date of  switched or  discontinuation | Had any claims of prenatal visits |
| Had hospitalization due to infections | 182 (5.3%) | 40 (2.7%) | 142 (7.2%) | Had principal/secondary diagnosis of infections. ((https://www.questdiagnostics.com/dms/Documents/Other/CPT-  2015/ICD\_9-10\_Infectious\_Disease\_MI4956.pdf) |
| Tuberculosis | 43 (1.2%) | 7 (0.5%) | 36 (1.8%) | ICD-9 codes 010-018, 137.0 or ICD-10 codes A15.7, A15.0, A15.8, A17.0, A18.01, A18.02, A18.03, A18.09, A18.4, A19.9, B90.9 |
| HBV | 6 (0.2%) | 1 (0.1%) | 5 (0.3%) | ICD-9 codes 070.32 or ICD-10 codes B18.1 |
| Herpes zoster | 3 (0.1%) | 0 (0%) | 3 (0.2%) | ICD-9 codes 053.9 or ICD-10 codes B02.9 |