Supplementary Tables

**Supplementary Table I. Baseline characterization according to gender at disease onset**

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| Characteristics | Total | Male | Female | Statistical test (males *vs* females) | P value |
| Number of Patients | 94 | 19 | 75 | - | - |
| Caucasian, n (%) | 86 (91) | 18 (95) | 68 (91) | Chi-square Test (CST) | 0.57 |
| Age (y) bDMARD started, median (IQR) | 56 (47 – 62) | 59 (54 – 66) | 55 (47 – 61) | Mann-Whitney-U – 2 tailed | 0.038 |
| (MWU) |
| Disease duration (y) from time of diagnosis to first bDMARD, median (IQR) | 4 (1 - 9) | 4 (1 - 8) | 3 (1 - 9) | MWU | 0.629 |
| Either or anti-CCP/RF positive, n (%) | 76 (81) | 16 (84) | 60 (80) | Fisher´s Exact Test (FET) | 0.513 |
| Anti-CCP/RF negative, n (%) | 18 (19) | 3 (16) | 15 (20) | FET | 0.513 |
| Methotrexate, n (%) | 82 (87) | 16 (84) | 66 (88) | FET | 0.448 |
| Methotrexate mg/day, median (IQR) | 20 (15 – 20) | 15 (12.5 – 20) | 20 (15 – 20) | MWU | 0.651 |
| Prednisolone, n (%) | 62 (66) | 11 (58) | 51 (68) | FET | 0.589 |
| Prednisolone equivalent mg/day, median (IQR) | 10 (5 – 12) | 10 (10 – 15) | 10 (5 – 10) | MWU | 0.820 |
| Pre-bDMARD DAS 28 – ESR, median (IQR), n | 5,31 (4,51 – 6,29) n=76 | 5,41 (4,53 – 5,87) n=13 | 5,31 (4,53 – 6,48) n=60 | MWU | 0.261 |
| Pre-bDMARD HAQ, median (IQR) | 2 (1,47 – 2,53) n=33 | 2,07(1,54 – 2,78) n=8 | 2 (1,5 – 2,5) n=25 | MWU | 0.220 |
| **Initial bDMARD:** | | | | | |
| Infliximab, n (%) | 3 (3) | - | 3 (4) | FET | 0.38 |
| Etanercept, n (%) | 55 (59) | 12 (63) | 43 (57) | CST | 0.65 |
| Adalimumab, n (%) | 14 (15) | 4 (21) | 10 (13) | FET | 0.40 |
| Golimumab, n (%) | 2 (2) | - | 2 (3) | FET | 0.47 |
| Tocilizumab, n (%) | 14 (15) | 3 (16) | 11 (15) | FET | 0.9 |
| Rituximab, n (%) | 6 (6) | - | 6 (8) | FET | 0.2 |
| **Comorbidities:** | | | | | |
| Benign Tumors n (%) | 4 (4) | 2 (11) | 2 (3) | FET | 0.181 |
| Dyslipidemia, n (%) | 48 (51) | 9 (47) | 39 (52) | FET | 0.8 |
| Arterial hypertension, n (%) | 39 (41) | 6 (32) | 33 (44) | FET | 0.436 |
| Chronic anxiety/depression disorder, n (%) | 18 (19) | 3 (16) | 15 (20) | FET | 1.00 |
| Active smoking, n (%) | 12 (16) | 3 (16) | 9 (12) | FET | 0.703 |
| Obesity, n (%) | 9 (10) | 4 (21) | 5 (7) | FET | 0.078 |
| Charlson Comorbidity Index at time bDMARD started, median (IQR) | 2 (2 -3) | 3 (3 – 4) | 2 (1 – 3) | MWU | 0.098 |
| Estimated 10-year survival at the time bDMARD started, median (IQR) | 90 (77 – 90) | 77 (53 – 77) | 90 (77 – 96) | MWU | 0.098 |

**Supplementary Table II. Recall characterization according to gender**

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| Characteristics at Recall | Total | Male (M) | Female (F) | Statistical test (M *vs* F) | P value |
| Number of Patients (%) | 77 | 14 (18) | 63 (82) | - | - |
| Age (y), median (IQR) | 63 (55 – 71) | 69 (58 – 77) | 62 (55 – 68) | MWU | 0.053 |
| Caucasian, n (%) | 71 (92) | 14 (100) | 57 (90) | FET | 0.585 |
| Anti-CCP, n (%) | 56 (73) | 11 (79) | 45 (72) | FET | 0.746 |
| Anti-RF, n (%) | 57 (74) | 9 (64) | 48 (76) | FET | 0.501 |
| Either or anti-CCP/RF positive, n (%) | 61 (79) | 11 (79) | 50 (79) | FET | 1.000 |
| Anti-CCP/RF negative, n (%) | 16 (21) | 3 (21) | 13 (21) | FET | 1.000 |
| Age (y) bDMARD started, median (IQR) | 56 (49 – 61) | 59 (53 – 68) | 55 (49 – 61) | MWU | 0.256 |
| Disease duration (y) from diagnosis to recall, median (IQR) | 12 (7 – 18) | 14 (11 – 17) | 12 (6 – 18) | MWU | 0.275 |
| Disease duration (y) from diagnosis to first bDMARD, median (IQR) | 4 (1 – 9) | 5 (2 – 9) | 4 (1 – 9) | MWU | 0.811 |
| Duration of follow-up from onset of bDMARD to recall, median (IQR) | 7 (4 – 9) | 7 (3 – 9) | 9 (7 – 9) | MWU | 0.079 |
| On bDMARD at recall, n (%) | 61 (79) | 8 (57) | 53 (84) | FET | 0.062 |
| Last bDMARD: |  |  |  |  |  |
| Etanercept, n (%) | 31 (51) | 4 (50) | 27 (51) | FET | 0.96 |
| Adalimumab, n (%) | 5 (8) | 1 (12) | 4 (7) | FET | 0.63 |
| Tocilizumab, n (%) | 15 (25) | 2 (25) | 13 (25) | FET | 0.98 |
| Infliximab, n (%) | 1 (1,5) | 0 | 1 (2) | FET | 0.7 |
| Rituximab, n (%) | 6 (10) | 1 (12) | 5 (9) | FET | 0.79 |
| Golimumab, n (%) | 2 (3) | 0 | 2 (4) | FET | 0.58 |
| Abatacept, n (%) | 1 (1,5) | 0 | 1 (2) | FET | 0.70 |
| Retained original bDMARD, n (%) | 46 (75) | 6 (75) | 40 (75) | FET | 1.00 |
| Compliance with bDMARD over the past year (n=56) | 45 (80) | 6 (85) | 39 (80) | FET | 0.70 |
| Had discontinued bDMARD by recall, n (%) | 16 (21) | 6 (43) | 10 (16) | FET | 0.062 |
| 1.     Primary failure to bDMARD | 2 (13) | 1 (17) | 1 (10) | FET | 0.457 |
| 2.     Secondary failure to bDMARD | 2(13) | 1 (17) | 1 (10) | FET | 0.333 |
| 3.     Infection | 6 (38) | 2 (33) | 4 (40) | FET | 0.298 |
| 4.     Neoplastic disease | 1(6) | 1(17) | 0 (0) | FET | 0.182 |
| 5.     Remission | 3 (19) | 1(17) | 2 (20) | FET | 0.457 |
| 6.     Other | 2 (13) | 0 (0) | 2 (20) | FET | 1.000 |
| Switched bDMARD, n (%)\* | 22 (29) | 4 (29) | 18 (29) | FET | 1.000 |
| 1.    Once | 14 (64) | 2 (14) | 12 (19) | FET | 1.000 |
| 2.    Twice | 6 (27) | 1 (7) | 5 (8) | FET | 1.000 |
| 3.    Thrice | 1 (5) | 1 (7) | 0 (0) | FET | 0.182 |
| 4.    Fourth | 1 (5) | 0 (0) | 1 (2) | FET | 1.000 |
| \*5 patients switched and stopped |  |  |  |  |  |
| Prior to bDMARD: |  |  |  |  |  |
| Pre bDMARD DAS 28 – ESR, median (IQR) n=72 | 5.060 (4.500 -5.998) | 5.105(4.595 – 5.800) | 5.060 (4.500 – 6.195) | MWU | 0.933 |
| Pre bDMARD HAQ, median (IQR) n=27 | 2.000 (1.440 – 2.490) | 2.375 (1.723 –2.840) | 1.938 (1.410 – 2.380) | MWU | 0.494 |
| Methotrexate, n (%) | 73 (95) | 14 (100) | 59 (94) | FET | 1.000 |
| Metotrexate dose mg/week, median (IQR) | 20 (13 – 20) | 14 (13 – 20) | 20 (15 – 20) | MWU | 0.220 |
| Steroids, n (%) | 57 (74) | 9 (64) | 48 (76) | FET | 0.501 |
| Prednisolone equivalent mg, median (IQR);  dose not known in 6 females and 2 males | 10 (5 – 10) | 10 (5 – 10) | 8 (5 – 10) | MWU | 0.564 |
| Recall: |  |  |  |  |  |
| Recall DAS 28 – ESR, median (IQR) n=72 | 3.200 (2.390 – 3.950) | 2.76 (1.765 – 3.905) | 3.2 (2.580 – 3.920) | MWU | 0.568 |
| Recall HAQ, median (IQR) n=77 | 1.250 (0.500 – 1.810) | 1.120 (0.500 – 1.470) | 1.310 (0.500 – 1.870) | MWU | 0.447 |
| Methotrexate, n (%) | 17 (22) | 3 (21) | 14 (22) | FET | 1.000 |
| Metotrexate dose mg/week, median (IQR) | 15 (10 – 20) | 15 (11 – 15) | 15 (11 – 20) | MWU | 0.400 |
| Steroids, n (% of 77) | 23 (30) | 3 (21) | 20 (36) | FET | 0.535 |
| Prednisolone equivalent mg/day, median (IQR) | 5 (5 – 10) | 5 (5 – 8) | 5 (5 – 11) | MWU | 1.00 |
| Steroids plus bDMARD, n (% of 61) | 16 (26) | 1 (12) | 15 (28) | FET | 0.668 |
| Steroids having discontinued bDMARD, n (% of 16) | 7 (43) | 2 (33) | 5 (50) | FET | 0.633 |
| Deformities, n (%) – 54 patients evaluated | 22 (41) | 6/10 (60) | 16/44 (36) | FET | 0.285 |
| Deformities/patient, median (IQR)\*\* | 0.5 (0 – 2.25) | 3 (0 – 7) | 0 (0 - 2) | MWU | 1.00 |
| Dyslipidemia, n (%) | 41 (53) | 7 (50) | 34 (54) | FET | 1.00 |
| Arterial hypertension, n (%) | 33 (43) | 7 (50) | 26 (41) | FET | 0.566 |
| Chronic anxiety/depression disorder, n (%) | 14 (18) | 0 | 14 (22) | FET | 0.061 |
| Active smoking, n (%) | 11 (14) | 0 | 11 (17) | FET | 0.199 |
| Obesity, n (%) | 8 (10) | 0 | 8 (13) | FET | 0.338 |
| Charlson comorbidity index at the time bDMARD started, median (IQR) | 2 (2 -3) | 3 (2.25 – 4.00) | 2 (2 – 3) | MWU | 0.019 |
| % Estimated 10 year survival at the time bDMARD started, median (IQR) | 90 (77 – 90) | 77 (53 - 86,75) | 90 (77 – 90) | MWU | 0.019 |
|  |  |  |  |  |  |
| EQ-5D 3L (n=76) |  |  |  |  |  |
| Mobility, mean (SD) | 1,72 (0.51) | 1.79 (0.58) | 1.70 (0.49) | T-test | 0.595 |
| Personal Care, mean (SD) | 1,65 (0.58) | 1.5 (0.65) | 1.69 (0.56) | T-test | 0.277 |
| Usual Activities, mean (SD) | 1,76 (0.59) | 1.64 (0.63) | 1.79 (0.58) | T-test | 0.399 |
| Pain and Unwell, mean (SD) | 1,97 (0.57) | 1.71 (0.61) | 2.03 (0.55) | T-test | 0.058 |
| Anxiety and Depression, mean (SD) | 1,72 (0.72) | 1.64 (0.63) | 1.74 (0.72) | T-test | 0.646 |
| EQ-5D 3L Visual Analogue Scale (VAS), mean (SD) | 60,64 (22.07) | 62.93 (24.21) | 60.11 (21.91) | T-test | 0.672 |
| EQ-5D 3L score –Portuguese tariff, mean (SD) | 0,45 (0.3) | 0.51 (0.39) | 0.43 (0.28) | T-test | 0.410 |
|  |  |  |  |  |  |

**Supplementary Table III. Pearson correlations between SF-36 and EQ-5D-3L parameters**

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
|  | | EQ-5D 3L - VAS | EQ-5D 3L tariff – adjusted for Portugal | PCS | MCS |
| EQ-5D 3L - VAS | Pearson Correlation | 1 | ,713\*\* | ,469\*\* | ,427\*\* |
| Sig. (2-tailed) |  | ,000 | ,002 | ,005 |
| N | 75 | 71 | 42 | 42 |
| EQ-5D 3L tariff – adjusted for Portugal | Pearson Correlation | ,713\*\* | 1 | ,424\*\* | ,499\*\* |
| Sig. (2-tailed) | ,000 |  | ,005 | ,001 |
| N | 71 | 73 | 42 | 42 |
| PCS | Pearson Correlation | ,469\*\* | ,424\*\* | 1 | -,096 |
| Sig. (2-tailed) | ,002 | ,005 |  | ,535 |
| N | 42 | 42 | 44 | 44 |
| MCS | Pearson Correlation | ,427\*\* | ,499\*\* | -,096 | 1 |
| Sig. (2-tailed) | ,005 | ,001 | ,535 |  |
| N | 42 | 42 | 44 | 44 |

\*\*Correlation is significant at the 0.01 level (2-tailed); \*Correlation is significant at the 0.05 level (2-tailed); Effect size Evans (1996): 00-0,19 “very weak”; 0,20-0,39 “weak”; 0,40-0,59 “moderate”; 0,60-0,79 “strong”; · 0,80-1.0 “very strong".

**Supplementary Table IV. Clinical parameters such as recall age, disease activity, functional status, EQ-5D Pt tariff, number of deformities, PCS and MCS with respect to professional situation, schooling and marital status**

|  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- |
|  |  | Age (years) | DAS28num | HAQ | EQ\_5D Pt tariff (D1 model) | Number of deformities | PCS | MCS |
| **Professional Situation** |  |  |  |  |  |  |  |  |
| Employed | Mean | 55,380 | 3,230 | 0,872 | 0,544 | 0,640 | 41,115 | 49,789 |
| N | 21 | 21 | 21 | 19 | 14 | 14 | 14 |
| Std. Deviation | 10,670 | 1,249 | 0,634 | 0,265 | 0,929 | 9,109 | 10,896 |
| Unemployed | Mean | 57,500 | 4,100 | 1,246 | 0,296 | 2,400 | 40,983 | 44,793 |
| N | 8 | 7 | 8 | 7 | 5 | 3 | 3 |
| Std. Deviation | 6,908 | 1,754 | 0,632 | 0,169 | 4,336 | 4,216 | 14,711 |
| Retired | Mean | 67,680 | 3,340 | 1,000 | 0,422 | 3,700 | 35,736 | 46,902 |
| N | 37 | 33 | 37 | 36 | 23 | 21 | 21 |
| Std. Deviation | 9,062 | 1,320 | 0,748 | 0,332 | 6,609 | 10,737 | 11,525 |
| Homemaker | Mean | 62,830 | 2,720 | 0,998 | 0,420 | 2,500 | 40,833 | 26,045 |
| N | 6 | 6 | 6 | 6 | 2 | 2 | 2 |
| Std. Deviation | 6,940 | 1,135 | 0,809 | 0,237 | 3,536 | 0,491 | 6,662 |
| **Schooling** |  |  |  |  |  |  |  |  |
| University Degree or Professional Equivalent | Mean | 63,230 | 3,290 | 0,978 | 0,558 | 1,360 | 43,708 | 42,932 |
|  | N | 13 | 13 | 13 | 12 | 11 | 7 | 7 |
|  | Std. Deviation | 12,370 | 0,901 | 0,639 | 0,276 | 2,541 | 13,715 | 12,121 |
| No University Degree | Mean | 62,140 | 3,280 | 1,239 | 0,418 | 2,820 | 36,613 | 47,583 |
| N | 63 | 58 | 63 | 60 | 34 | 36 | 36 |
| Std. Deviation | 10,171 | 1,450 | 0,747 | 0,295 | 5,681 | 8,341 | 11,588 |
| **Marital Status** |  |  |  |  |  |  |  |  |
| Single | Mean | 51,770 | 2,940 | 1,199 | 0,378 | 2,750 | 34,808 | 49,709 |
|  | N | 13 | 13 | 13 | 11 | 8 | 6 | 6 |
|  | Std. Deviation | 9,722 | 1,425 | 0,743 | 0,267 | 5,825 | 4,183 | 13,895 |
| Married | Mean | 63,630 | 3,540 | 1,150 | 0,443 | 2,040 | 38,657 | 46,309 |
| N | 43 | 40 | 43 | 42 | 26 | 22 | 22 |
| Std. Deviation | 9,991 | 1,430 | 0,733 | 0,307 | 2,891 | 11,099 | 11,319 |
| Divorced | Mean | 62,920 | 3,240 | 1,428 | 0,431 | 5,330 | 35,250 | 49,074 |
| N | 11 | 9 | 11 | 10 | 6 | 8 | 8 |
| Std. Deviation | 5,862 | 1,383 | 0,795 | 0,223 | 11,219 | 7,045 | 12,519 |
| Widow | Mean | 70,780 | 2,670 | 1,110 | 0,518 | 0,800 | 40,391 | 43,412 |
| N | 9 | 9 | 9 | 9 | 5 | 7 | 7 |
| Std. Deviation | 7,293 | 0,584 | 0,702 | 0,361 | 0,837 | 10,552 | 11,382 |

**Supplementary Table V. Comparison of patients who died with recall cohort**

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| **Characteristics** | Died | Recall | Statistical test (dead *vs* alive) | P value |
| Number of Patients | 6 | 77 |  |  |
| Age (y) patient, median (IQR) | 66 (61 – 67) | 63 (55 – 71) | MWU | 0.398 |
| Caucasian, n (%) | 6 (100) | 71 (92) | FET | 1.000 |
| Anti-CCP, n (%) | 4 (67) | 56 (73) | FET | 0.667 |
| Anti-RF, n (%) | 5 (83) | 57 (74) | FET | 1.000 |
| Either or anti-CCP/RF positive, n (%) | 6 (100) | 61 (79) | FET | 0.591 |
| Age (y) bDMARD started, median (IQR) | 61 (57 – 64) | 56 (49 – 61) | MWU | 0.190 |
| Disease duration (y) from diagnosis, median (IQR) | 16 (8 – 21) | 12 (7 – 18) | MWU | 0.342 |
| Disease duration (y) from diagnosis to bDMARD, median (IQR) | 7 (3 – 11) | 4 (1 – 9) | MWU | 0.321 |
| Duration of follow-up from onset of bDMARD, median (IQR) | 5 (3 – 6) | 7 (4 – 10) | MWU | 0.331 |
| Had discontinued bDMARD, n (%) | 4 (67) | 16 (21) | FET | 0.028 |
| Comorbidities: | | | | |
| Active smoking, n (%) | 1 (17) | 1 (14) | FET | 1.00 |
| Dyslipidemia, n (%) | 5 (83) | 41 (53) | FET | 0.218 |
| Arterial hypertension, n (%) | 4 (67) | 33 (43) | FET | 0.4 |
| Obesity, n (%) | 0 | 8 (10) | FET | 1.00 |
| Chronic anxiety/depression disorder, n (%) | 1 (17) | 14 (18) | FET | 1.00 |
| Charlson comorbidity index at the time bDMARD started, median (IQR) | 4 (3 – 5) | 2 (2 – 3) | MWU | 0.006 |
| % Estimated 10-year survival at time bDMARD started, median (IQR) | 65 (29 – 77) | 90 (77 - 90) | MWU | 0.006 |