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**Do TNF Inhibitors Reduce the Incidence of Cardiac, Pulmonary and Neurologic Comorbidities in Ankylosing Spondylitis? An Analysis of Three Large US Claims Databases.**

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**Background:** Patients with ankylosing spondylitis, a multi-system immune-mediated chronic inflammatory disease, have experienced reduction in signs and symptoms, improvement in physical function and quality of life with the advent of biologic treatments such as tumor necrosis factor inhibitors (TNFi). Whether TNFi have altered the incidence of comorbidities in AS is not known.

**Methods:** Three commercial insurance claims databases – Multi-Payer Claims Database (MPCD) (2007-2010), Truven Marketscan (2010-2014), and the U.S. Medicare Fee-for-Service Claims data (2006-2014) – were searched to assess disease manifestations (uveitis, psoriasis, and inflammatory bowel disease) and comorbidities (cardiac, neurological, kidney, lung diseases) in three groups of AS patients: those managed with either no therapy or prescription non-steroidal anti-inflammatory drugs (NSAIDs), those given conventional disease modifying anti-rheumatic drugs (DMARDS), and those using TNFi. Entry criteria were a rheumatologist’s diagnosis of AS, six-months of pre-diagnosis insurance coverage, and (for drug-specific exposures) administration of AS exposures of interest after the AS diagnosis. For the estimation of the incidence of comorbidities, data collection ended at the earliest of date of death, loss of medical or pharmacy coverage, end of study period, first outcome occurrence, or treatment discontinuation. Samples of the non-AS general population in Medicare was used as comparator.

**Results:** Total number of people included in three databases is ≈ 40 million. The age & sex standardized prevalence of AS was XX. The prevalence of comorbidities and disease manifestations by treatment exposures stratified by each data source are shown in Table 1. The incidence rates of outcome of interest by treatment exposures stratified by each data source are shown in Table 2a and 2b.

**Table 1:** The prevalence of comorbidities and disease manifestations by per 100 treatment exposures stratified by each data source

|  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **Specific manifestation** | **MPCD** | | | **Marketscan** | | | **Medicare** | | |
| **TNF** | **DMARD** | **NSAIDS or no exposure** | **TNF** | **DMARD** | **NSAID or no exposure** | **TNF** | **DMARD** | **NSAID or no exposure** |
| Aortic Insufficiency | 1.5 | 0.8 | 2.0 | 1.8 | 2.1 | 2.8 | 8.0 | 10.9 | 11.7 |
| Conduction Block | 0.4 | 0.8 | 0.8 | 1.7 | 2.4 | 2.5 | 6.8 | 8.6 | 10.5 |
| Myocardial infarction | 0.3 | NA | 0.5 | 0.5 | 0.5 | 0.5 | 1.7 | 1.9 | 2.4 |
| Crohn’s Disease | 6.1 | 4.2 | 2.9 | 6.4 | 4.8 | 3.3 | 10.4 | 8.8 | 5.8 |
| Ulcerative Colitis | 3.7 | 3.1 | 2.0 | 4.9 | 3.0 | 2.6 | 7.4 | 7.2 | 4.9 |
| Amyloidosis | NA | NA | 0.0 | 0.0 | 0.0 | 0.0 | 0.1 | 0.1 | 0.2 |
| IgA nephropathy | 0.1 | 0.2 | 0.1 | 0.2 | 0.2 | 0.1 | 0.7 | 0.9 | 0.6 |
| Nephrotic syndrome | 0.0 | 0.0 | 0.0 | 0.1 | 0.1 | 0.1 | 0.2 | 0.5 | 0.3 |
| Apical Pulmonary fibrosis | NA | NA | 0.0 | 0.0 | NA | 0.0 | 0.0 | 0.1 | 0.0 |
| Interstitial lung disease | 0.2 | NA | 0.0 | 0.1 | 0.2 | 0.1 | 0.3 | 0.5 | 0.2 |
| Restrictive lung disease | 1.0 | 0.6 | 1.6 | 3.9 | 4.4 | 4.7 | 15.5 | 20.1 | 18.0 |
| Cauda Equina syndrome | NA | NA | 0.1 | 0.1 | 0.2 | 0.1 | 0.2 | 0.3 | 0.3 |
| Spinal Cord compression | 0.1 | NA | 0.3 | 0.3 | 0.5 | 0.5 | 1.7 | 2.0 | 2.4 |
| Psoriasis | 4.1 | 2.5 | 2.7 | 5.1 | 3.8 | 2.3 | 9.9 | 8.0 | 5.8 |
| Psoriatic arthritis | 6.6 | 4.8 | 2.4 | 8.5 | 6.2 | 2.9 | 13.9 | 10.1 | 5.4 |
| Uveitis | 11.3 | 8.5 | 7.4 | 13.4 | 11.0 | 11.2 | 13.4 | 10.1 | 8.0 |

**Table 2a:** Incidence Rates of comorbidities and disease manifestations per 100 patient-years by treatment exposures stratified by each data source

|  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
|  | **MPCD Database** | | | **Marketscan Database** | | | **Medicare Database** | | |
|  | TNFi | NSAIDs/No Rx | p Value | TNFi | NSAIDs/No Rx | p Value | TNFi | NSAIDs/No Rx | p Value |
| **Aortic Insufficiency** | 1.3 | 1.9 | NS | 1.2 | 2.1 | 0.000 | 3.2 | 6.0 | 0.000 |
| **Conduction Block** | 0.3 | 0.9 | 0.03 | 1.1 | 2.4 | 0.000 | 2.9 | 5.9 | 0.000 |
| **Myocardial Infarction** | 0.3 | 0.6 | NS | 0.2 | 0.6 | 0.000 | 0.7 | 1.5 | 0.000 |
| **Restrictive Lung Disease** | 0.9 | 2.0 | 0.008 | 1.9 | 3.2 | 0.000 | 5.9 | 8.7 | 0.000 |
| **Spinal Cord Compression** | 0.1 | 0.3 | NS | 0.3 | 0.5 | 0.01 | 0.4 | 0.8 | 0.000 |
| **Psoriasis** | 3.5 | 1.6 | 0.000 | 3.8 | 1.8 | 0.000 | 3.8 | 2.1 | 0.000 |
| **Crohn’s Disease** | 4.7 | 3.0 | 0.006 | 4.8 | 2.6 | 0.000 | 3.9 | 2.5 | 0.000 |
| **Ulcerative Colitis** | 2.5 | 1.6 | 0.05 | 3.1 | 2.1 | 0.000 | 2.4 | 1.8 | 0.000 |
| **Uveitis** | 5.0 | 4.9 | NS | 7.6 | 8.0 | NS | 5.0 | 3.0 | 0.000 |

**Table 2b:** Incidence Rates of comorbidities and disease manifestations per 100 patient-years by treatment exposures stratified by each data source

|  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
|  | **MPCD Database** | | | **Marketscan Database** | | | **Medicare Database** | | |
|  | TNFi | DMARD | p Value | TNFi | DMARD | p Value | TNFi | DMARD | p Value |
| **Aortic Insufficiency** | 1.3 | 0.5 | 0.132 | 1.2 | 1.5 | 0.279 | 3.2 | 4.7 | 0.000 |
| **Conduction Block** | 0.3 | 0.0 | 0.286 | 1.1 | 1.4 | 0.473 | 2.9 | 4.2 | 0.000 |
| **Myocardial Infarction** | 0.3 | 0.0 | 0.286 | 0.2 | 0.3 | 0.568 | 0.7 | 1.2 | 0.000 |
| **Restrictive Lung Disease** | 0.9 | 0.0 | 0.029 | 1.9 | 2.4 | 0.190 | 5.9 | 7.7 | 0.000 |
| **Spinal Cord Compression** | 0.1 | 0.0 | 0.779 | 0.3 | 0.4 | 0.341 | 0.4 | 0.5 | 0.373 |
| **Psoriasis** | 3.5 | 1.0 | 0.003 | 3.8 | 3.3 | 0.397 | 3.8 | 3.4 | 0.161 |
| **Crohn’s Disease** | 4.7 | 3.6 | 0.365 | 4.8 | 4.1 | 0.276 | 3.9 | 3.7 | 0.605 |
| **Ulcerative Colitis** | 2.5 | 0.9 | 0.041 | 3.1 | 3.2 | 0.816 | 2.4 | 2.6 | 0.472 |
| **Uveitis** | 5.0 | 6.5 | 0.228 | 7.6 | 8.6 | 0.200 | 5.0 | 3.8 | 0.000 |

**Conclusion**: This analysis of three large insurance claims databases show that patients with AS on TNFi have lower incidence of certain cardiac, pulmonary and neurologic comorbidities, but higher incidence of some disease manifestations (uveitis, psoriasis and IBD), compared to those treated with NSAIDs alone.