Individual Project Proposal

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CS-6440 – Introduction to Health Informatics

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Clinical Question

In patients undergoing treatment for auto-immune disorders who are prescribed biologics, does Adalimumab (brand name Humira) or Etanercept (brand name Enbrel) have an increased risk of low platelet count (Thrombocytopenia) over the other?

As powerful treatments for Psoriasis, Arthritis, and other auto-immune disorders, biologics have become increasingly common use, though they often come with significant side effects. Thrombocytopenia is one of the most notable. In regards to both planned surgeries and sudden catastrophic events, Thrombocytopenia can be very dangerous for patients. Determining which of these biologics are more likely to cause a reduced platelet count would allow for minimizing a potentially deadly side effect, particularly in at-risk patient populations.

Background

Humira was approved in 2002 by the FDA in order to treat a host of auto-immune disorders, such as Rheumatoid Arthritis, Crohn's Disease, Psoriasis, and Ulcerative Colitis [1]. Enbrel had previously been approved in 1998 for a slightly more limited array of similar conditions [2].

A case study in 2006 documented a patient taking Enbrel who fell from 271 x 10^9 /l platelets to 38 x 10^9 /l [3]. Other similar studies have repeatedly shown that both of these drugs can induce thrombocytopenia—interestingly, despite actually being prescribed to treat refractory immune thrombocytopenia purpura [4]. In 2010, a study by Austrian researchers was published that raised this conflict, while also continuing to document patients taking Enbrel developing drug-induced thrombocytopenia [4].

For Humira, the same pattern has held. In 2012 a study was published discussing the case of "severe […] induced thrombocytopenia" in a Crohn's patient [5], while in 2016 a study demonstrated the same for a patient with severe psoriatic arthritis [6].

Surprisingly, I could not locate any studies that directly compare different biologic medications. However, a 2009 article published on Medscape referenced a study that was at least partly delineated by individual drug, which found an interesting variation based on the drugs— with the now recalled Raptiva (Efalizumab) not resulting in any cases of thrombocytopenia despite being the most tested for the study (n = 51), while all other drugs brought the general rate of occurrence of thrombocytopenia up to 4.3% (n = 93) [7]. Unfortunately, this study had a very small sample for Humira (n = 2), which makes it difficult to draw any conclusions from [7].

Cohorts

Target Cohort - The target cohort is patients who have taken Humira with at least 60 days of follow-up who did not have thrombocytopenia prior to starting the medication.

Comparator Cohort - The target cohort is patients who have taken Enbrel with at least 60 days of follow-up who did not have thrombocytopenia prior to starting the medication.

Outcome Cohort – The outcome cohort is patients who have been diagnosed with thrombocytopenia.

Additional Comments

Thrombocytopenia is defined by the American Academy of Family Physicians (AAFP) as a platelet count below 150 x 10^3 /μL [8]. While ideally the study would be performed on any relative drop in platelet count regardless of it reaches the threshold for thrombocytopenia, this is not possible with the data available. Without access to their bloodwork history to determine relative drops in platelet counts, **patients who have thrombocytopenia prior to starting one of the medications will also thus be excluded**. This should also inherently exclude patients taking the medication for refractory immune thrombocytopenia purpura [4]. It is likely that some patients have a relative platelet drop compared to their history prior to taking the medication that will not be included in the data.

It should be noted that due to the nature of thrombocytopenia often going unreported for the purposes of billing, it is not believed that the data will be a complete look at even just patients who explicitly reach thrombocytopenia status versus the general population. This should be a statistically even rate between the medications however, and as such this should not affect the relative data generated as it relates to the comparison of the medications.

References

[1] Humira (adalimumab) FDA Approval History. (n.d.). Retrieved from https://www.drugs.com/history/humira.html

[2] Enbrel (etanercept) FDA Approval History. (n.d.). Retrieved from https://www.drugs.com/history/enbrel.html

[3] Pathare, S. K., Heycock, C., & Hamilton, J. (2006). TNF blocker-induced thrombocytopenia. *Rheumatology*, *45*(10), 1313–1314. doi: 10.1093/rheumatology/kel204

[4] Brunasso, A., Laimer, M., & Massone, C. (2010). Paradoxical Reactions to Targeted Biological Treatments: A Way to Treat and Trigger? *Acta Dermato Venereologica*, *90*(2), 183–185. doi: 10.2340/00015555-0777

[5] Casanova, M., Chaparro, M., Martínez, S., Vicuña, I., & Gisbert, J. (2012). Severe adalimumab-induced thrombocytopenia in a patient with Crohns disease. *Journal of Crohns and Colitis*, *6*(10), 1034–1037. doi: 10.1016/j.crohns.2012.04.001

[6] Pereira VC, Costa KH, de Oliveira LR (2016) Chronic Use of Adalimumab as Potential Cause of Severe Thrombocytopenia in Psoriatic Arthritis Patient: The Need for Regular Monitoring of Cytopenias. *Int J Blood Res Disord*, 3(1). Retrieved from https://clinmedjournals.org/articles/ijbrd/international-journal-of-blood-research-and-disorders-ijbrd-3-020.pdf

[7] Thrombocytopenia Associated With the Use of Anti-Tumor Necrosis Factor-α Agents for Psoriasis. (2009, July 9). Retrieved from https://www.medscape.com/viewarticle/705156

[8] Gauer, R., & Braun, M. M. (2012, March 15). Thrombocytopenia. Retrieved from https://www.aafp.org/afp/2012/0315/p612.html