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CADTH Reference List

Infliximab for Graft-Versus-Host Disease

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Summary of Abstracts

CADTH

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About CADTH: CADTH is an independent, not-for-profit organization responsible for providing Canada's health care decision-makers with objective evidence to help make informed decisions about the optimal use of drugs, medical devices, diagnostics, and procedures in our health care system.

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Key Message

Three non-randomized studies were found about the benefits and harms of Infliximab for graft-versus-host disease.

Research Question

What are the benefits and harms of Infliximab for graft-versus-host disease?

Methods

Literature Search Methods

A limited literature search was conducted by an information specialist on key resources including MEDLINE, Embase, the Cochrane Database of Systematic Reviews, the International HTA Database, the websites of Canadian and major international health technology agencies, as well as a focused internet search. The search strategy comprised both controlled vocabulary, such as the National Library of Medicine's MeSH (Medical Subject Headings), and keywords. The main search concepts were infliximab and graft-versus-host disease. CADTH-developed search filters were applied to limit retrieval to health technology assessments, systematic reviews, meta-analyses, indirect treatment comparisons, any types of clinical trials or observational studies. Where possible, retrieval was limited to the human population. The search was completed on June 10, 2022 and limited to English-language documents published since January 1, 2012. Internet links were provided, where available.

Selection Criteria and Summary Methods

One reviewer screened literature search results (titles and abstracts) and selected publications according to the inclusion criteria presented in Table 1. Full texts of study publications were not reviewed. The Overall Summary of Findings was based on information available in the abstracts of selected publications.

Results

Three non-randomized studies[1-3] were identified about the benefits and harms of Infliximab for graft-versus-host disease. No relevant health technology assessments, systematic reviews, or randomized controlled trials were identified.

Additional references of potential interest that did not meet the inclusion criteria are provided in Appendix 1.

Table 1: Selection Criteria

Criteria	Description
Population	Patients (of all ages) with graft-versus-host disease.
Intervention	Infliximab with or without other interventions
Comparator	Other interventions (i.e., extracorporeal photopheresis, mycophenolate mofetil, etanercept, low-dose methotrexate, mTOR inhibitor [e.g., sirolimus, everolimus], imatinib, ibrutinib, rituximab, pentostatin, cyclosporine, corticosteroids), placebo, no treatment
Outcomes	Clinical effectiveness (e.g., failure-free survival, overall response rate, health-related quality of life, symptom severity, duration of response, overall survival, non-relapse mortality, malignancy relapse or progression, steroid dosing); safety (e.g., adverse events, severe adverse events)
Study designs	Health technology assessments, systematic reviews, randomized controlled trials, non-randomized studies

mTOR = mechanistic target of rapamycin.

Overall Summary of Findings

Three non-randomized studies were identified about the benefits and harms of infliximab for graft-versus-host disease (GvHD).[1-3] Two studies[1,2] that retrospectively examined individuals who were treated with infliximab for steroid-refractory acute GvHD found that the number of individuals who responded to treatment decreased over time. One study[2] found that most individuals developed infectious complications within 12 weeks and that most deaths within 6 months were secondary to complications from GvHD or infections. Researchers concluded that infliximab was associated with a modest and poorly sustained effect and an increased risk of severe infection.[2] The other study[1] concluded that individuals who responded to infliximab early on had a significantly higher chance of overall survival compared to non-responders.

One study[3] retrospectively examined individuals treated with a combination of basiliximab and infliximab for acute GvHD and found that most individuals responded to treatment after 21 days. After 1 year, researchers found an overall survival rate of 24% and noted that most deaths were due to complications from GvHD and recurrence of the primary disease.[3] Researchers concluded that this intervention was not more effective than other treatments for GvHD and was less effective than basiliximab alone.[3]

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References

Health Technology Assessments

No literature identified.

Systematic Reviews

No literature identified.

Randomized Controlled Trials

No literature identified.

Non-Randomized Studies

Single Arm Studies

1. Nygaard M, Andersen NS, Moser CE, et al. Evaluation of infliximab as second-line treatment of acute graft versus host disease -validating response on day 7 and 28 as predictors of survival. *Bone Marrow Transplant.* 07 2018; 53(7): 844-851. PubMed
2. Yalniz FF, Hefazi M, McCullough K, et al. Safety and Efficacy of Infliximab Therapy in the Setting of Steroid-Refractory Acute Graft-versus-Host Disease. *Biol Blood Marrow Transplant.* Sep 2017; 23(9): 1478-1484. PubMed
3. Nadeau M, Perreault S, Seropian S, Foss F, Isufi I, Cooper DL. The use of basiliximab-infliximab combination for the treatment of severe gastrointestinal acute GvHD. *Bone Marrow Transplant.* Feb 2016; 51(2): 273-6. PubMed

Appendix 1: References of Potential Interest

Previous CADTH Reports

4. Infliximab for Graft Versus Host Disease. *(CADTH reference list: summary of abstracts).* Ottawa (ON):CADTH; 2022: https://www.cadth.ca/infliximab-graft-versus-host-disease. Accessed 2022 Jun 16.

Systematic Reviews

Mixed Intervention – Not Specific to Infliximab

5. Rashidi A, DiPersio JF, Sandmaier BM, Colditz GA, Weisdorf DJ. Steroids Versus Steroids Plus Additional Agent in Frontline Treatment of Acute Graft-versus-Host Disease: A Systematic Review and Meta-Analysis of Randomized Trials. *Biol Blood Marrow Transplant.* 06 2016; 22(6): 1133-1137. PubMed

Conference Abstracts

6. Dignan F, Velickovic V, McIlwaine E, Zhang R, Spelman T. Adverse effects of therapeutic treatments for acute graft versus host disease (aGvHD): a systematic review. *Bone Marrow Transplantation*. 2019; 53: 392-393.

7. Taylor A, Wissinger E, Cadarette S, Ruiz K, Jansson J, Akbari M. Treatments for steroid-refractory acute graft versus host disease: a systematic literature review. *HemaSphere*. 2018 June; 2(Supplement 2): 1087.

Non-Randomized Studies

Conference Abstracts

8. Jansen SA, Verbeek AB, von Asmuth EGJ, Muskens KF, Buddingh EP, Lindemans CA. Abstract: 373. Age Is a Risk Factor for Mortality in Pediatric Steroid-Refractory Acute Graft-Versus-Host Disease: A Multicenter Study. Presented at the 2022 Tandem Meetings, the combined annual meetings of ASTCT and CIBMTR: Salt Lake City (UT). 2022 Apr 23-26: https://tandem.confex.com/tandem/2022/meetingapp.cgi/Paper/18893. Accessed 2022 Jun 17.

9. Cavness A, Jacobsohn DA, Rohatgi R. Safety and Efficacy of Twice-Weekly Versus Once-Weekly Infliximab for Refractory Acute Graft-Versus-Host Disease in Pediatric Patients. *Biol Blood Marrow Transplant*. 2020 March; 26(3 Supplement): S391.

10. Agrawal V, Griffin SP, Koch L, et al. Outcomes of Infliximab in Management of Steroid-Refractory Acute Graft Versus Host Disease. *Biol Blood Marrow Transplant*. 2019 March; 25(3 Supplement): S249-S250.

11. Nygaard M, Karlsmark T, Smedegaard N, et al. Experience with the use of infliximab and/or extracorporeal photopheresis in steroid-refractory acute graft versus host disease. *Biol Blood Marrow Transplant*. 2018 March; 24(3 Supplement 1): S194.

Review Articles

12. Jamil MO, Mineishi S. State-of-the-art acute and chronic GVHD treatment. *Int J Hematol.* 2015; 101(5): 452-466. PubMed
See: Anti-TNFα agents (page 457)

Additional References

13. NHS England Specialised Services Clinical Reference Group for Blood and Marrow Transplantation. Clinical Commissioning Policy: Treatments for Graft versus Host Disease (GvHD) following Haematopoietic Stem Cell Transplantation. Leeds (UK): NHS England; 2017: https://www.england.nhs.uk/wp-content/uploads/2017/03/gvhd-heamatopoietic-stem-cell.pdf. Accessed 2022 Jun 16.
See: Infliximab (page 15-16)