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Argumentation based synthesis: an illustrative example

Neil Hawkins PhD Cstat, University of Glasgow, UK

Argumentation based synthesis

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Aggregating evidence about the positive and negative effects of treatments

Anthony Hunter[a,*], Matthew Williams[b]

[a] Department of Computer Science, University College London, London WC1E 6BT, UK
[b] Department of Clinical Oncology, University College Hospital, London NW1 2PG, UK

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ABSTRACT

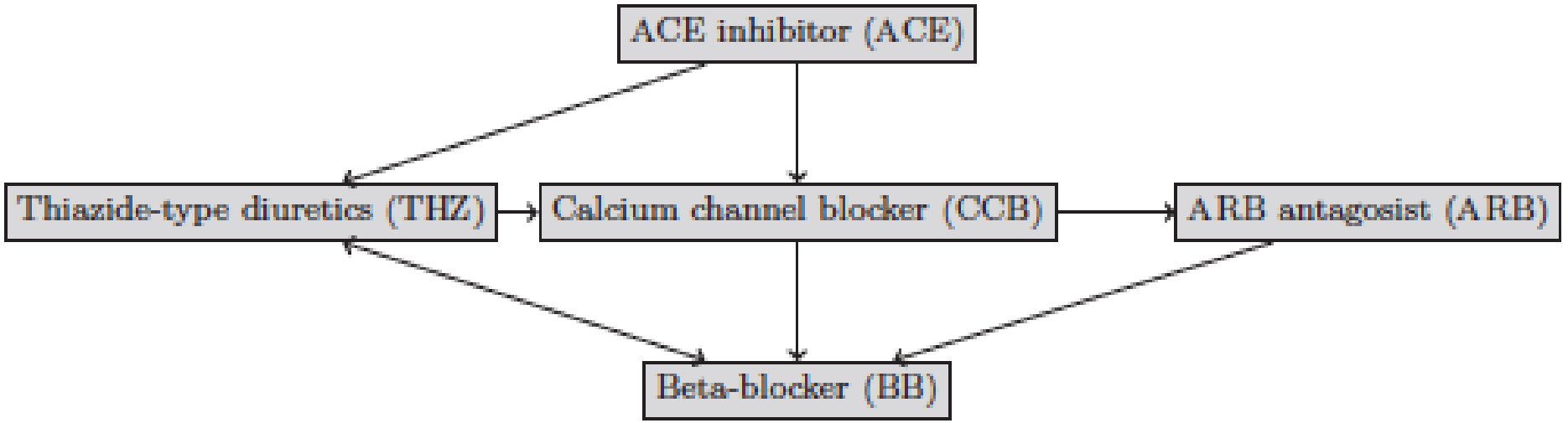
Objectives: Evidence-based decision making is becoming increasingly important in healthcare. Much valuable evidence is in the form of the results from clinical trials that compare the relative merits of treatments. In this paper, we present a new framework for representing and synthesizing knowledge from clinical trials involving multiple outcome indicators.
Method: The framework generates and evaluates arguments for claiming that one treatment is superior, or equivalent, to another based on the available evidence. Evidence comes from randomized clinical trials, systematic reviews, meta-analyses, network analyses, etc. Preference criteria over arguments are used that are based on the outcome indicators, and the magnitude of those outcome indicators, in the evidence. Meta-arguments attacks arguments that are based on weaker evidence.
Results: We evaluated the framework with respect to the aggregation of evidence undertaken in three published clinical guidelines that involve 56 items of evidence and 16 treatments. For each of the three guidelines, the treatment we identified as being superior using our method is a recommended treatment in the corresponding guideline.
Conclusions: The framework offers a formal approach to aggregating clinical evidence, taking into account subjective criteria such as preferences over outcome indicators. In the evaluation, the aggregations obtained showed a good correspondence with published clinical guidelines. Furthermore, preliminary computational studies indicate that the approach is viable for the size of evidence tables normally encountered in practice.

Table of arguments

Table 1
Four results obtained from the NICE Hypertension Guideline (GC34, pages 36–37) concerning angiotensin-converting inhibitors (ACE) and calcium channel blockers (CCB).

	Left	Right	Outcome indicator	Value	Net	Sig	Type
e_1	ACE	CCB	Mortality	1.04	<	No	MA
e_2	ACE	CCB	Stroke	1.15	<	Yes	MA
e_3	ACE	CCB	Heart failure	0.84	>	Yes	MA
e_4	ACE	CCB	Diabetes	0.85	>	Yes	MA

Superiority Graph



1st Line Treatment for Chronic myelogenous Leukemia (CML)

- **CML** form of leukemia characterized by the increased and unregulated growth of myeloid cells in the bone marrow and the accumulation of these cells in the blood. Typically related to a specific mutation (Philadelphia chromosome)

- First Line Treatments
  - **Imatinib**
  - Bosutinib
  - **Nilotinib**
  - **Dasatinib**

- Effectiveness Endpoint
  - Major Molecular Remission (MMR)

Published NMA

First-line treatment strategies for newly diagnosed chronic myeloid leukemia: a network meta-analysis

This article was published in the following Dove Press journal:
Cancer Management and Research

Kang-Kang Chen[1]
Tai-Feng Du[1]
Ku-Sheng Wu[2]
Wei Yang[3]

[1]Department of Preventive Medicine and MPH Education Center, Shantou University Medical College, Shantou, Guangdong Province, China; [2]Department of Preventive Medicine, Shantou University Medical College, Shantou, Guangdong Province, China; [3]Department of Thoracic Surgery, Administrative Office, Shantou University Medical College Cancer Hospital, Shantou, Guangdong Province, China

Objectives: With bosutinib proven to be available for frontline treatment, there are currently four frontline treatments as well as an additional strategy with high-dose imatinib for newly diagnosed chronic myeloid leukemia (CML). Due to the lack of direct comparison of high-dose imatinib, dasatinib, nilotinib, and bosutinib, we summarized the evidence to indirectly compare the efficacy among these treatment options.

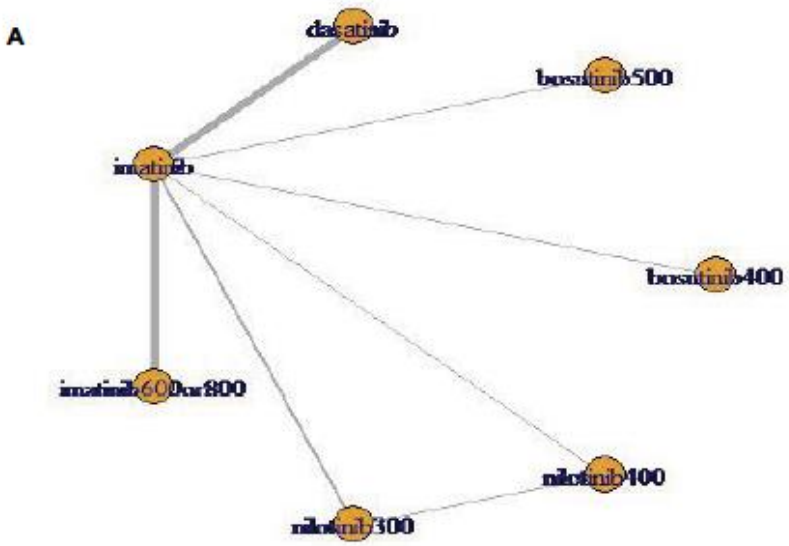
Methods: In total, 14 randomized clinical trials including 5,630 patients were analyzed by direct and mixed-treatment comparisons. Outcomes assessed were the following: complete cytogenetic response at 12 months; major molecular response at 12, 24, and 36 months; deep molecular response at 12, 24, 36, and 60 months; early molecular response at 3 months; progression-free survival (PFS); overall survival (OS); and Grade 3 or 4 adverse events (AEs).

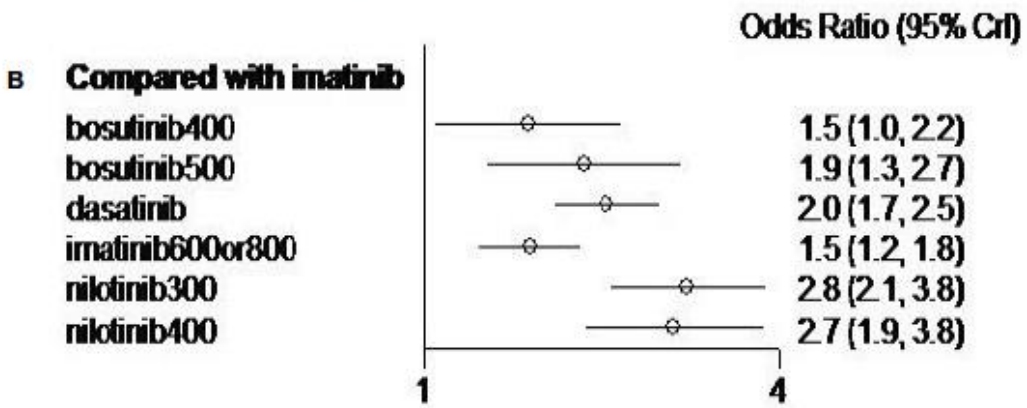
Results: The Bayesian network meta-analysis demonstrated that high-dose imatinib was less effective than all new-generation tyrosine kinase inhibitors and had a higher probability of Grade 3 or 4 AEs. For molecular response, 300 mg of nilotinib was likely to be the preferred frontline treatment, as demonstrated by higher response rates and faster, deeper, and longer molecular response. For PFS and OS, there were high likelihoods (79% and 74%, respectively) that 400 mg of nilotinib was the preferred option. For AEs, standard-dose imatinib has the highest probability (65%) of being the most favorable toxicity profile.

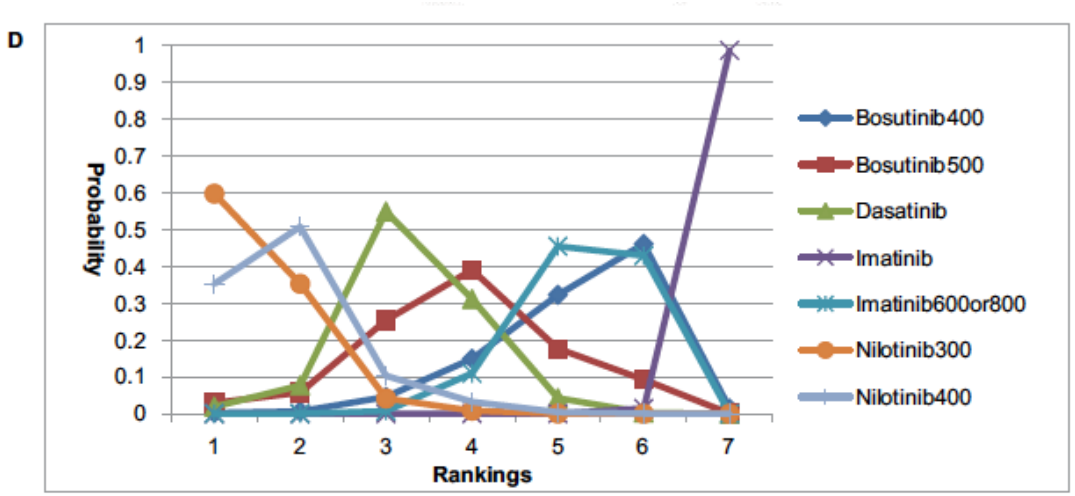
Conclusion: Considering the efficacy and toxicity profile, it is not recommended to use high-dose imatinib for treatment. This analysis also showed that nilotinib has the highest probability to become the preferred frontline agents for treating CML.

Keywords: CML, tyrosine kinase inhibitor, imatinib, bosutinib, dasatinib, nilotinib

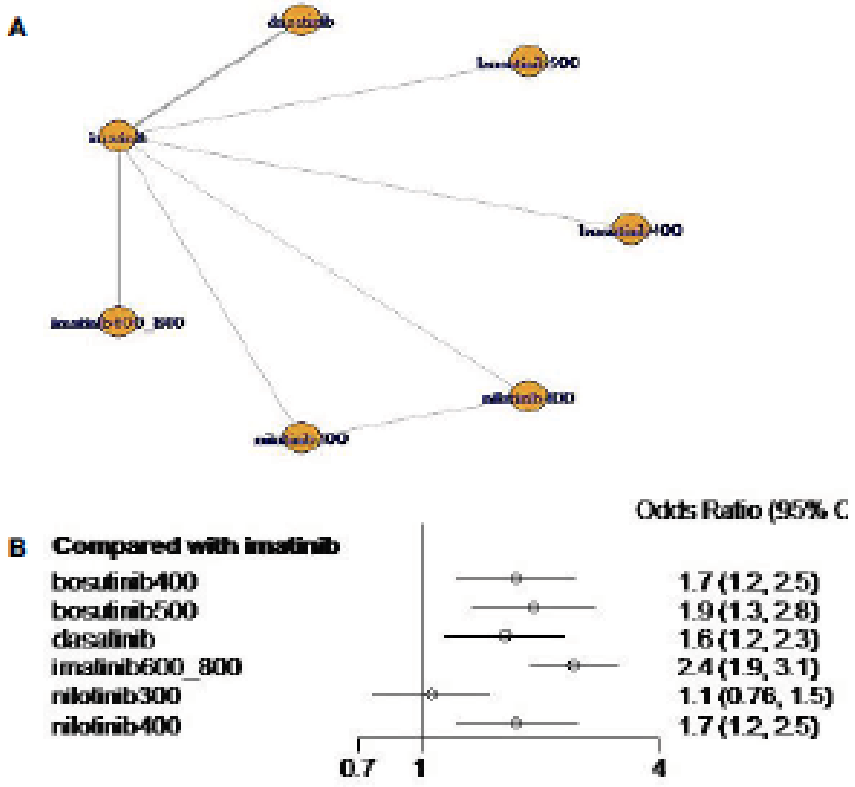
MMR at 12 Months

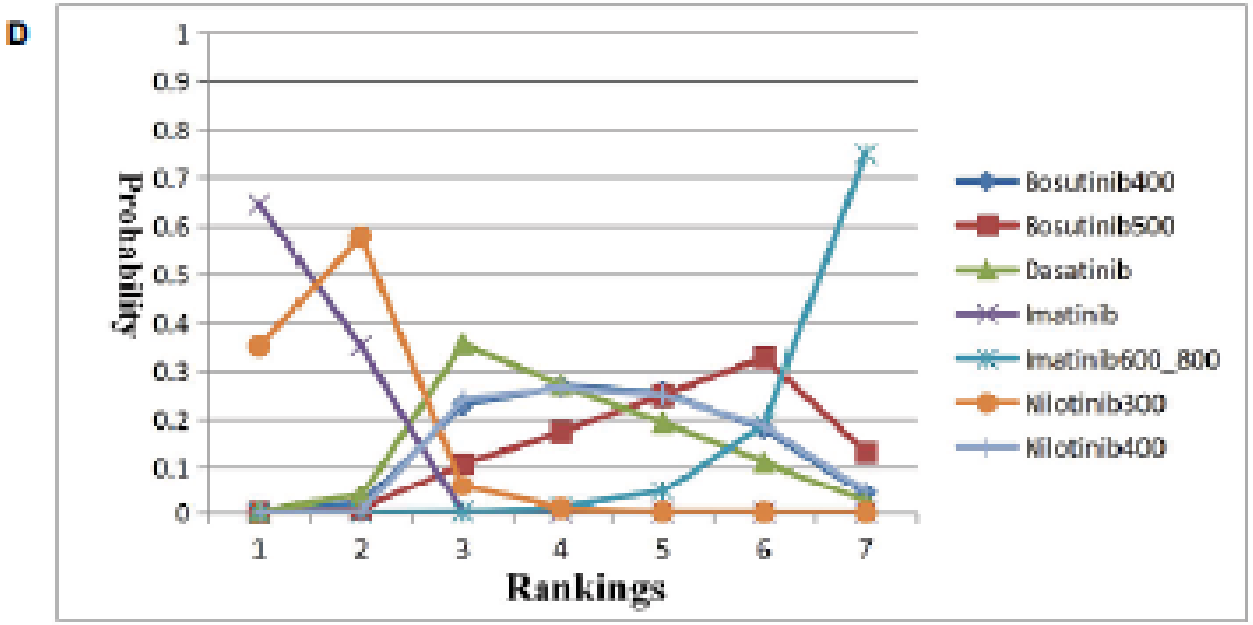




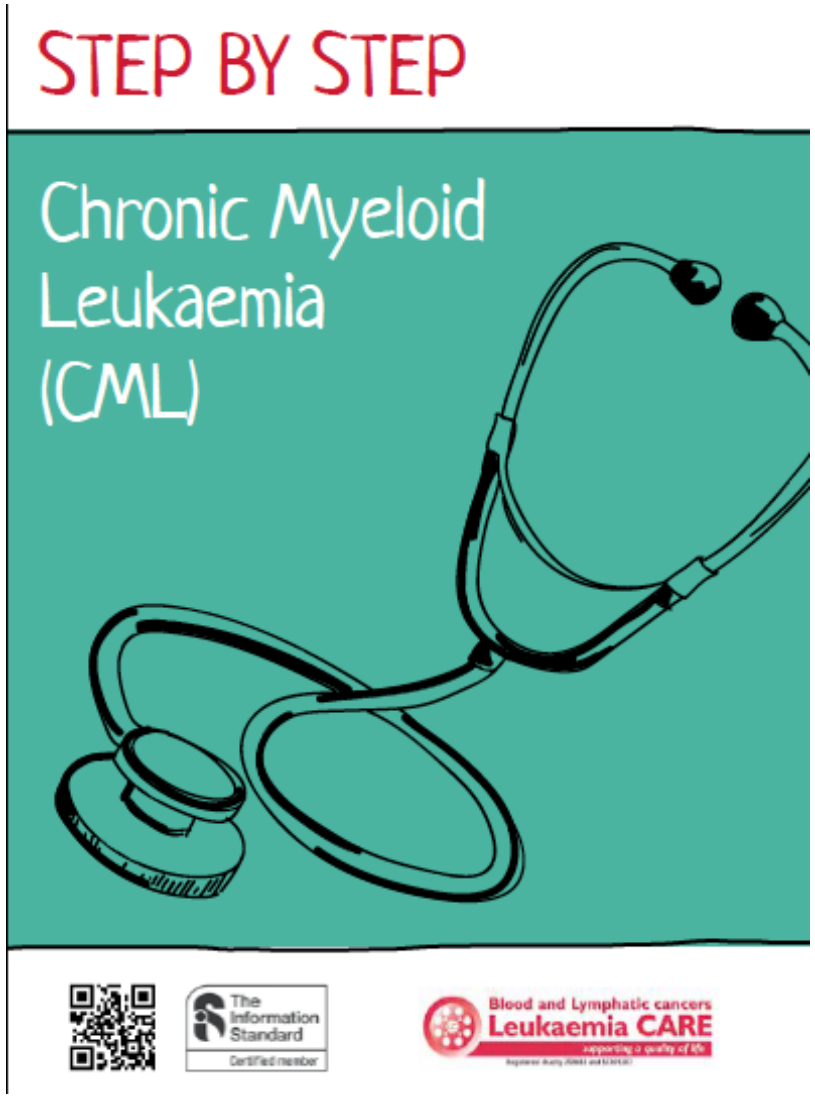


Grade 3 or 4 AEs





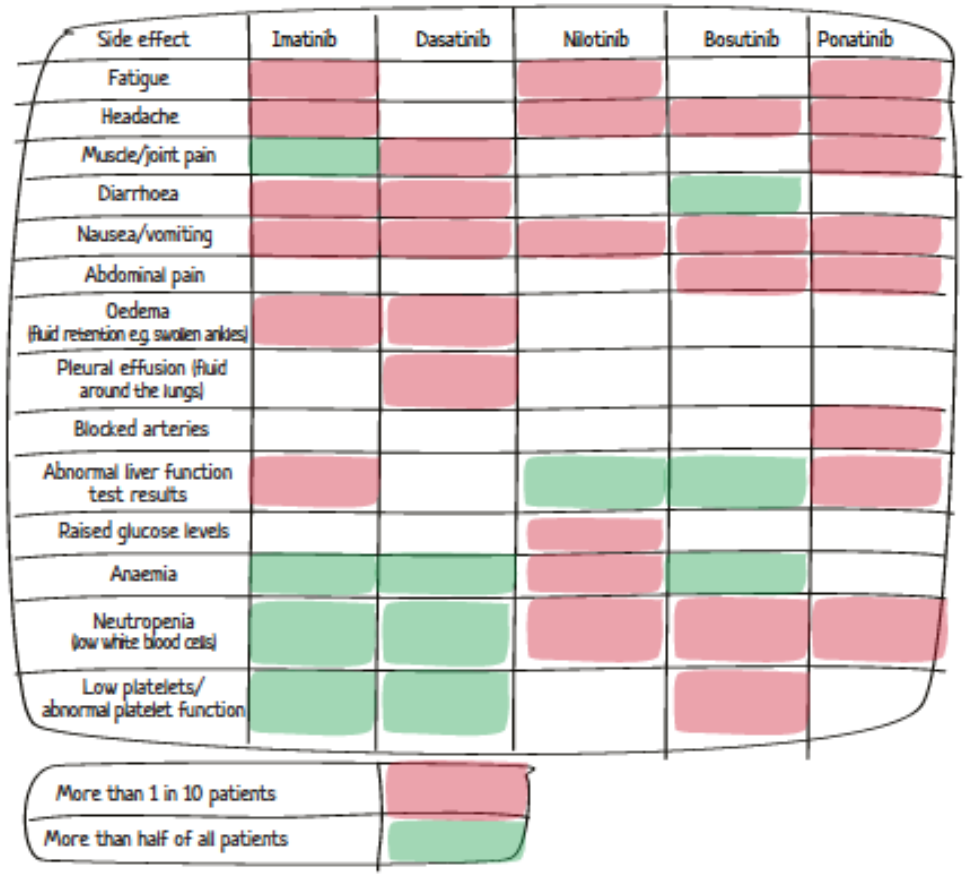
Patient information leaflet



Comparison between treatments

"Some of the side effects weren't nice; upset stomach, bone pains and tiredness. But as this drug was going to keep me alive, I was going to stick with it."

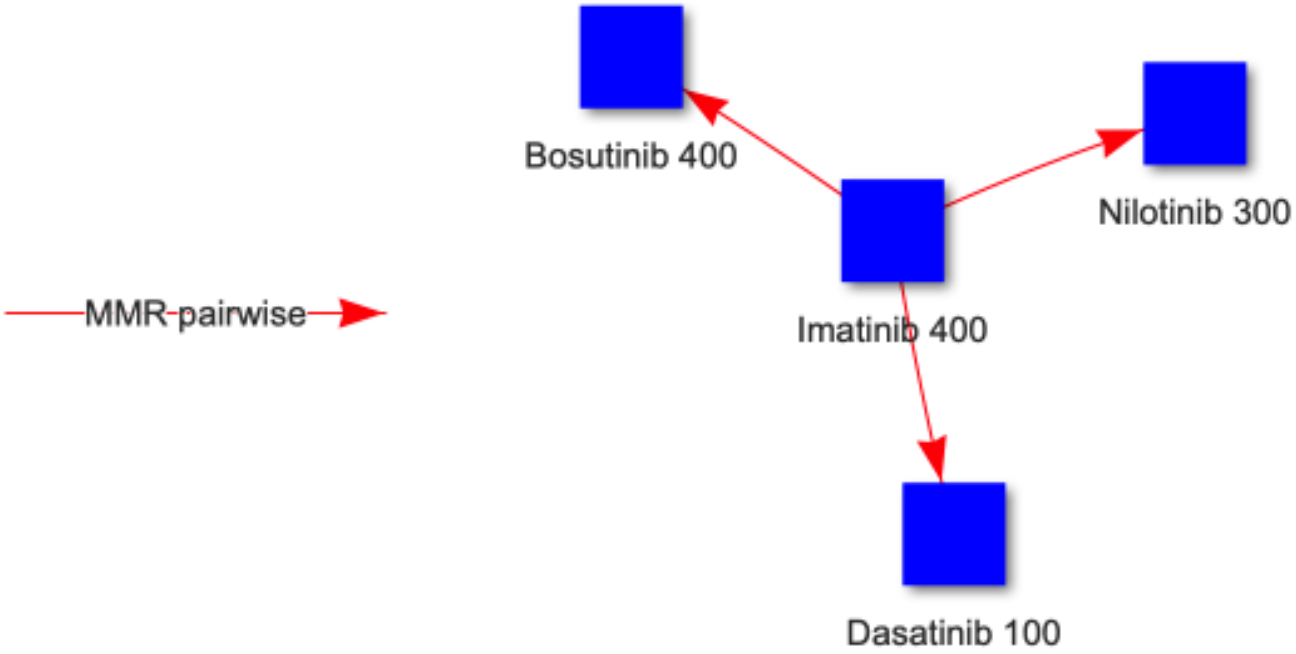
Remember to mention any side effects you're experiencing to your healthcare team as they will be able to help manage them.



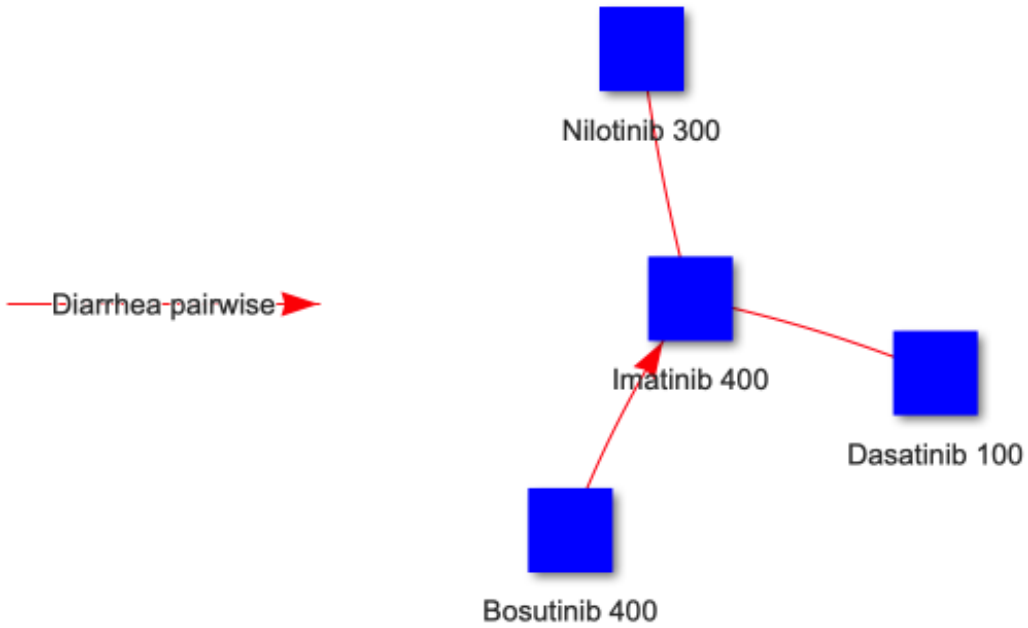
How useful are these to patients

- Network Meta-Analysis
  - Assumes consistency $OR_{AB}=OR_{AC}/OR_{BC}$
  - No material differences in treatment effect modifiers
  - Too much information, not patient focused
  - Clear link to underlying studies
- Parient leaflet
  - (Too) concise information, patient focused
  - Assumes naïve indirect comparisons valid
  - No material differences in treatment effect modifiers or prognostic factors
  - No clear link to underlying studies
- Argumentation based synthesis?

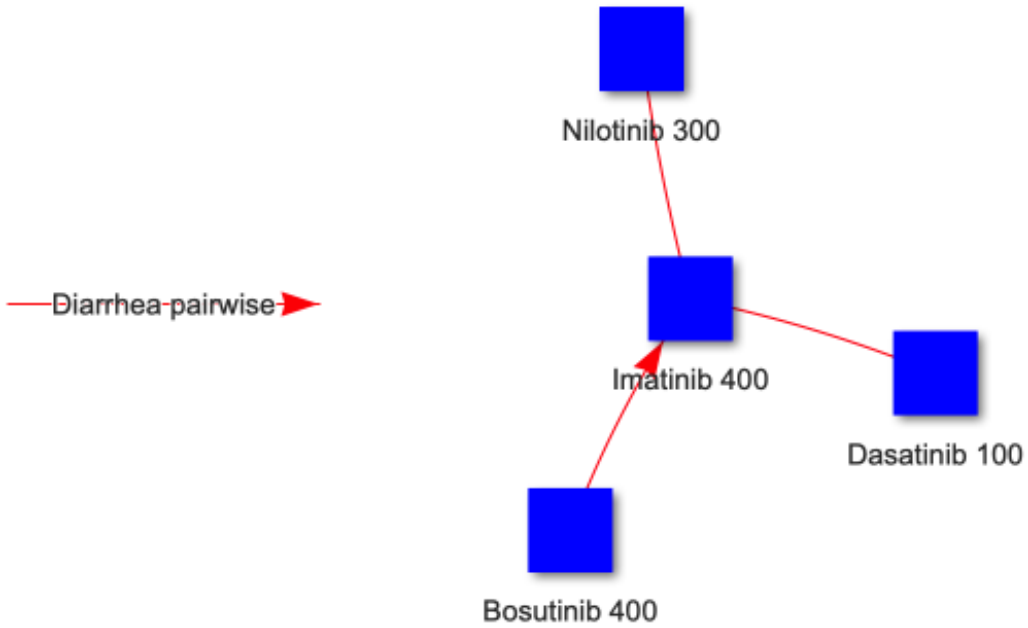
Arguments based on trial comparisons (P<0.05) for MMR



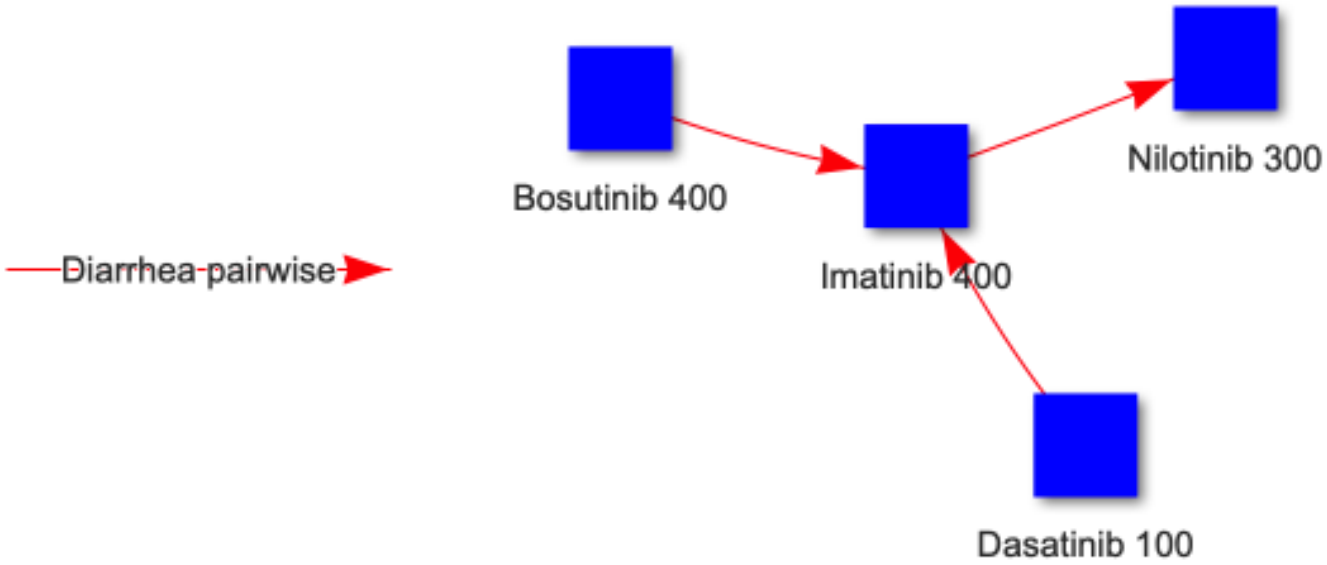
Arguments based on trial comparisons for ((P<0.05) P<0.05) Diarrhea



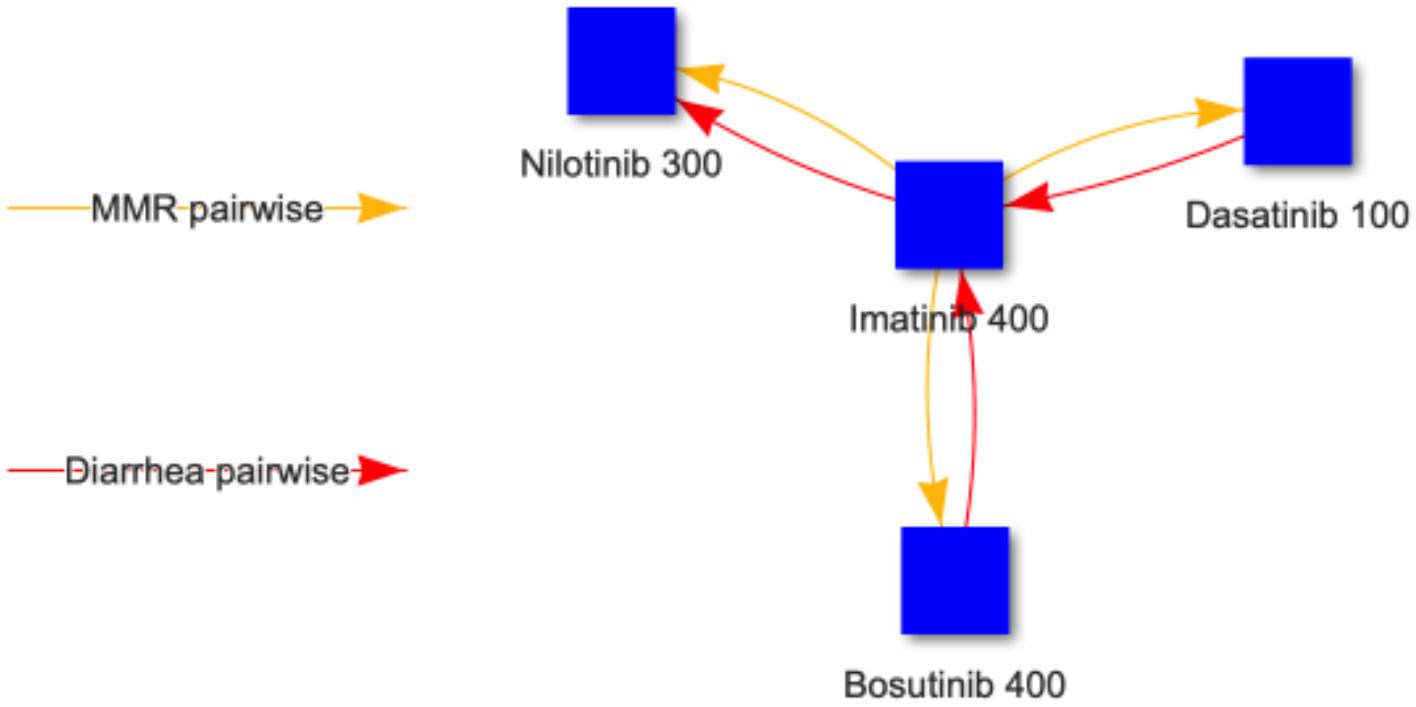
Arguments based on trial comparisons for ((P<0.05) P<0.05) Diarrhea



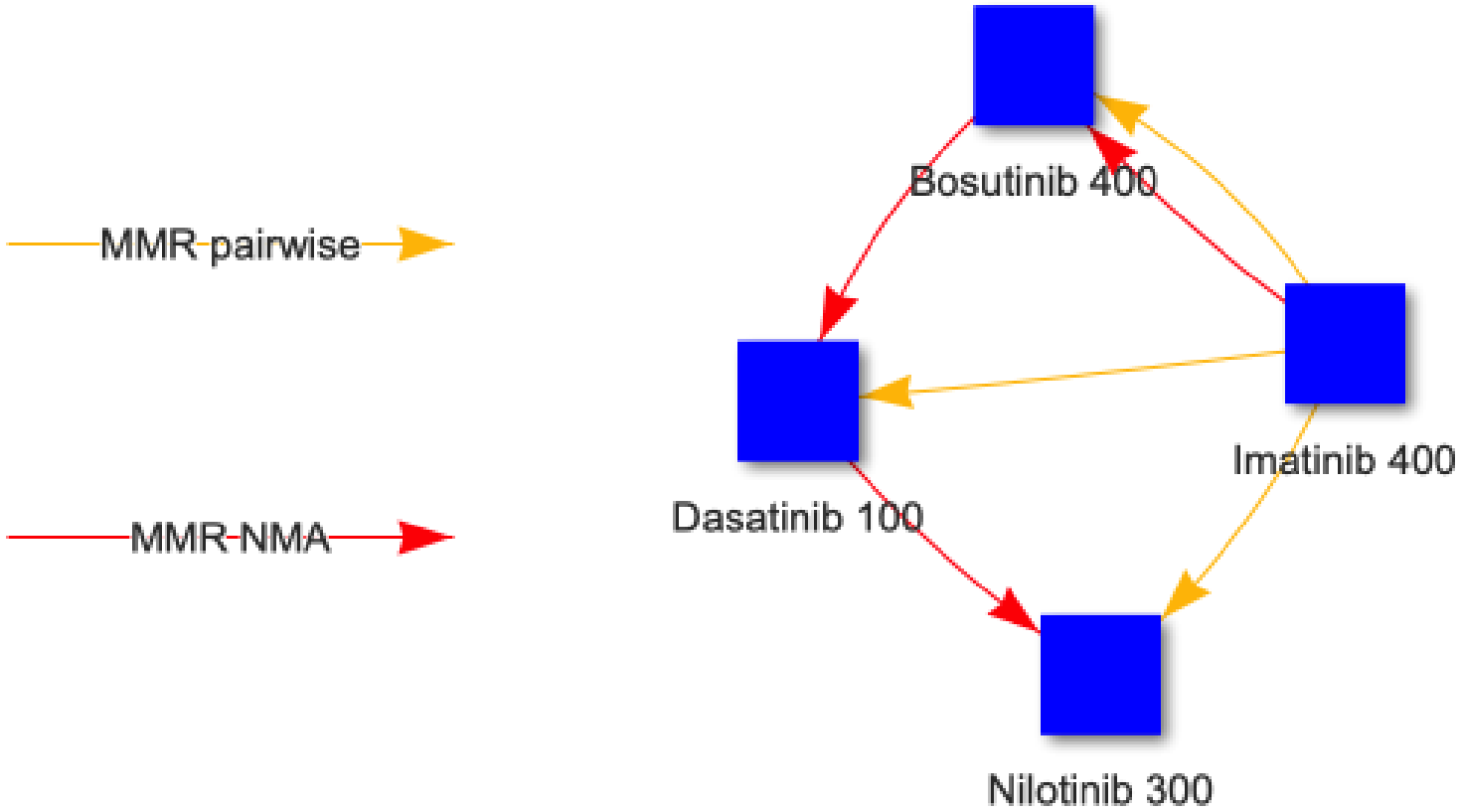
Arguments based on trial comparisons for Diarrhea



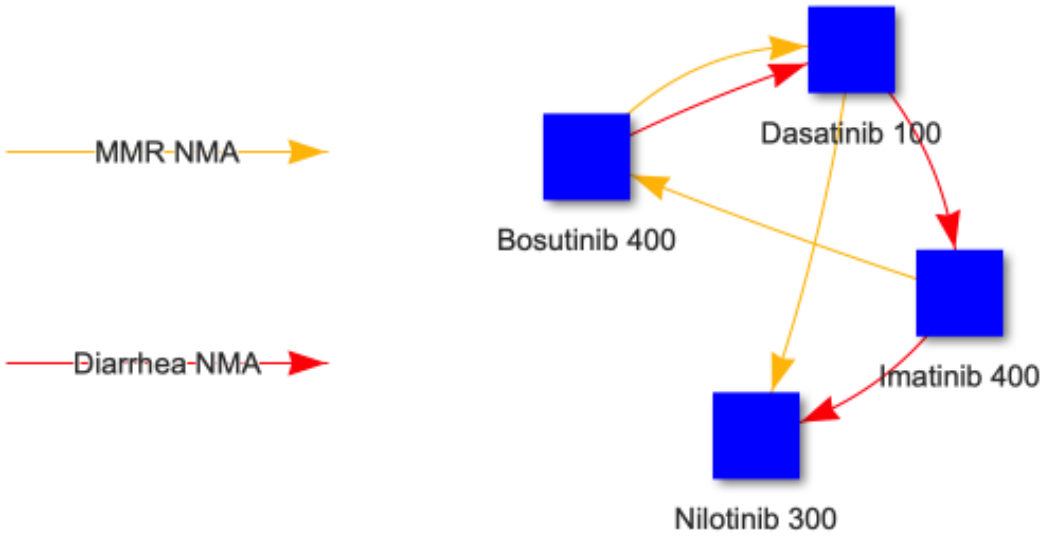
Comparison of arguments based on trial comparisons for Diarrhea and MMR



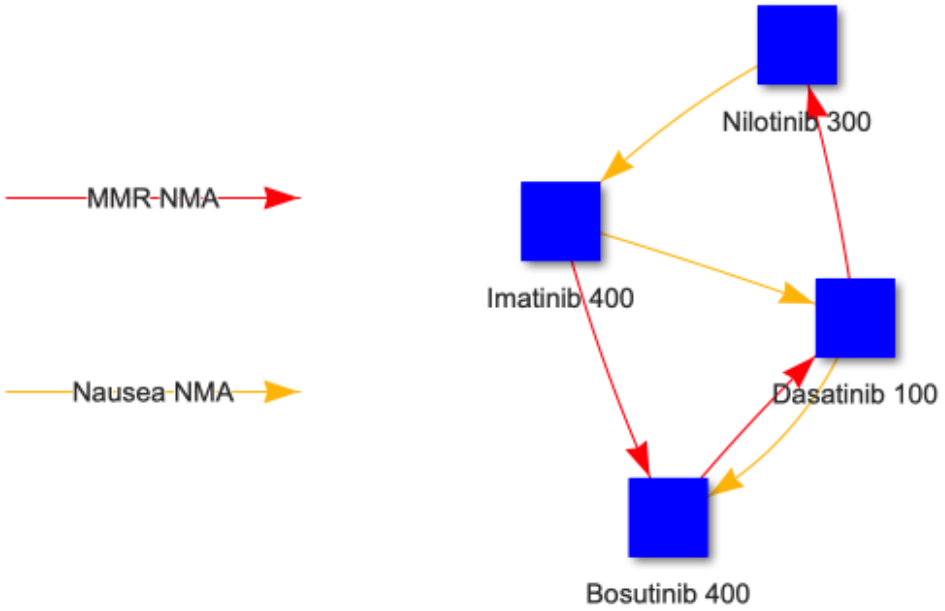
Arguments based on NMA and trial comparisons for MMR



Arguments based on NMA for MMR and Diarrhea



Arguments based on NMA for MMR and Nausea



Next Steps

- Indicate magnitude of effects to allow patients to make trade-offs
- Interactive app to allow patients to focus on what matters to them