PROTECT

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Pharmacoepidemiological Research on Outcomes of Therapeutics by a European Consortium

AGGREGATED DATA DRUG INFORMATION SYSTEM (ADDIS)
AN EVIDENCE-BASED DECISION SUPPORT SYSTEM FOR THE BENEFIT-RISK ASSESSMENT OF MEDICAL PRODUCTS

IMI-PROTECT Symposium

Benefit-Risk Integration and Representation Workshop

18th February 2015

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Disclaimer

"The processes described and conclusions drawn from the work presented herein relate solely to the testing of methodologies and representations for the evaluation of benefit and risk of medicines.

This report neither replaces nor is intended to replace or comment on any regulatory decisions made by national regulatory agencies, nor the European Medicines Agency."

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The 3 pillars of structured decision making

- Well-defined and transparent process
  - PrOACT-URL (EMA benefit-risk methodology project)
- Guidance on how to conduct the various steps in this process
  - IMI PROTECT benefit-risk group recommendations report
  - IMI PROTECT website and training materials
- Supporting software
  - ADDIS

ADDIS – a brief history

- The development of ADDIS started in 2009 as part of work package 3.2 of the Escher project
- This has resulted in the development of ADDIS 1
- ADDIS 2 is a web-based redevelopment of the previous prototype desktop application
- ADDIS 2 is currently still under heavy development but the software in now becoming useable as an analytical tool
- Both ADDIS 1 and 2 are open source and freely accessible from our website www.drugis.org

ADDIS 2: functional perspective

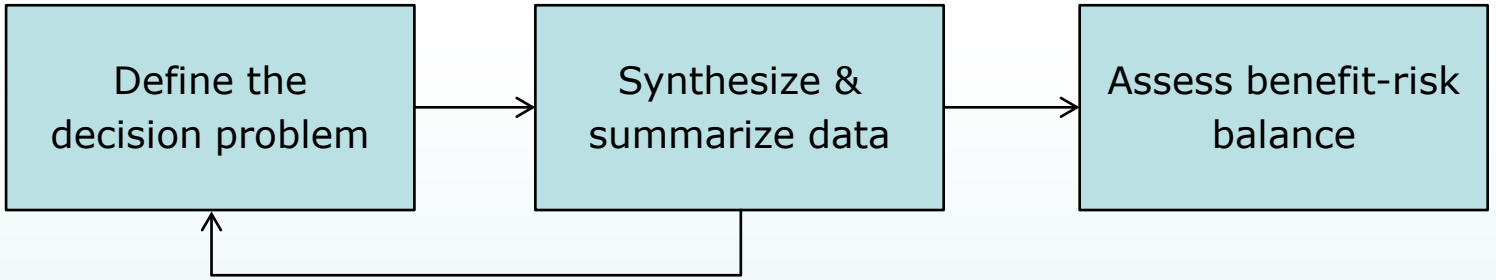
Quantitative methods

(network) meta-analysis

MCDA/SMAA

Disease progression modelling

Workflow



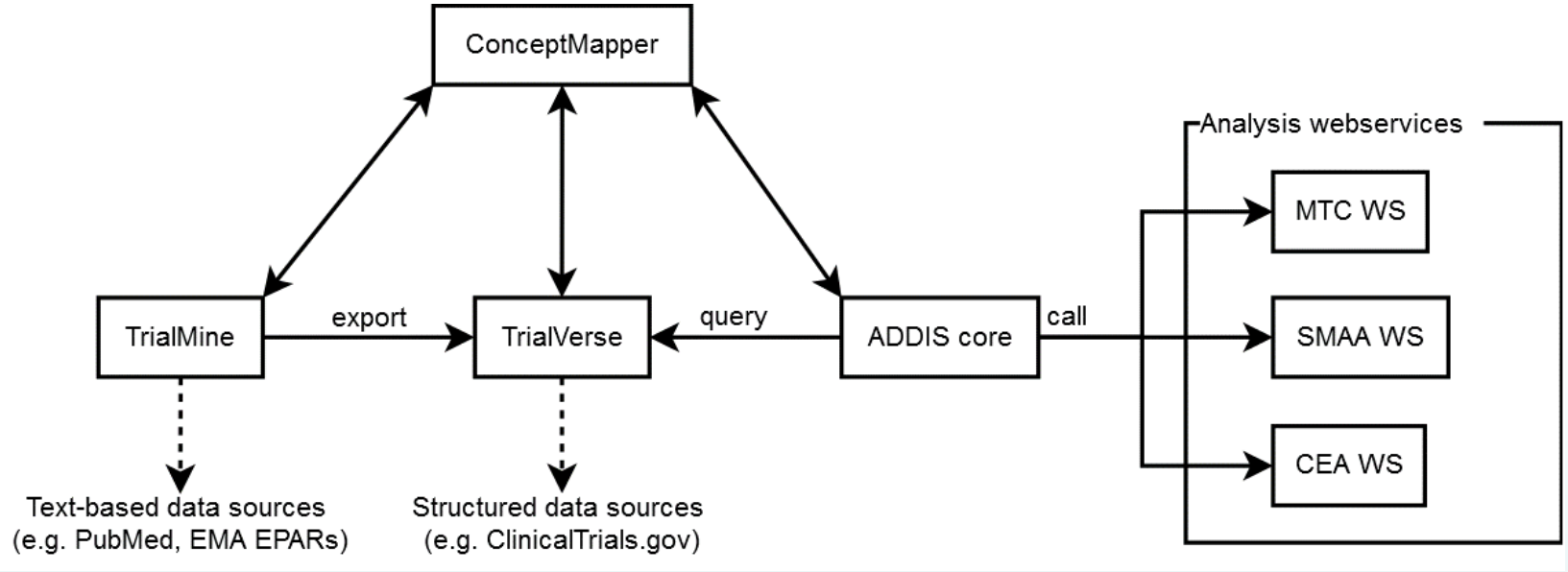
Visualisations

Value tree

Effects table

SMAA descriptive indices

ADDIS 2: technical perspective



MCDA WEB INTERFACE

Illustrative case study

EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

27 June 2013
EMA/CHMP/403683/2013
Committee for Medicinal Products for Human Use (CHMP)

Assessment report

Stivarga

International non-proprietary name: REGORAFENIB

Procedure No. EMEA/H/C/002573/0000

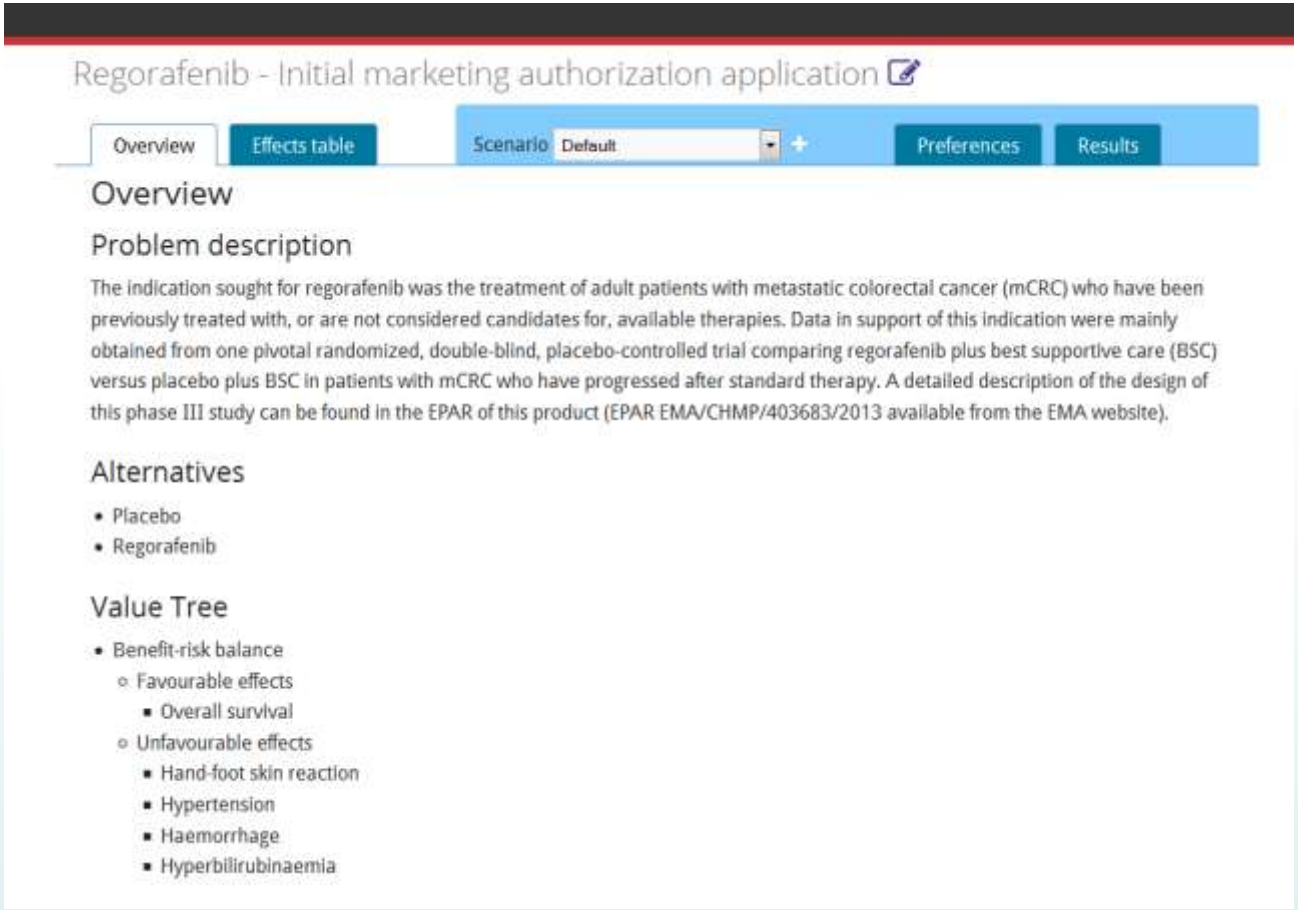
Note

Assessment report as adopted by the CHMP with all information of a commercially confidential nature deleted.

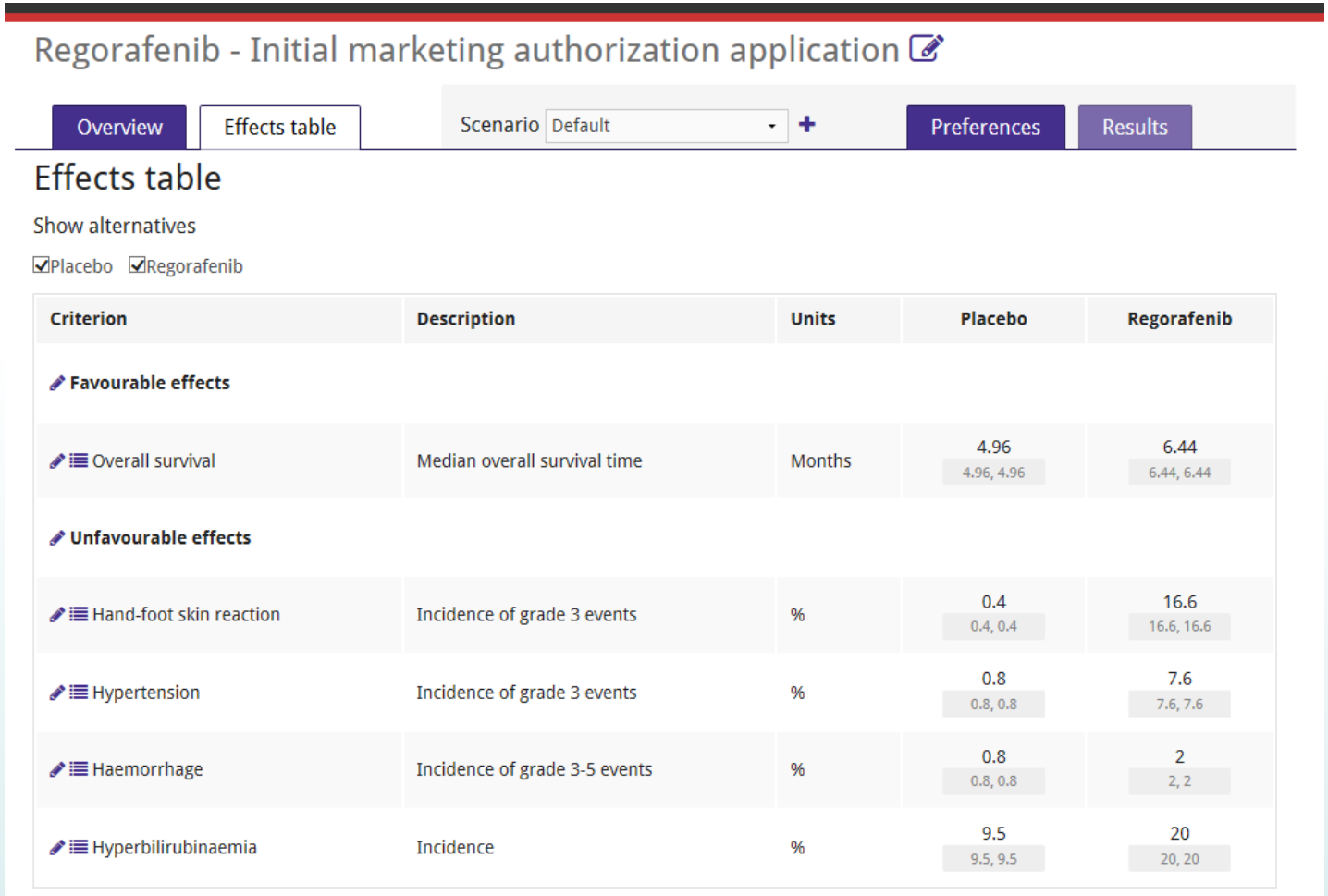
EMA/CHMP/403683/2013 Page 1/91

- We consider the problem of assessing the benefit-risk balance of regorafenib using the data available at the time of the initial marketing authorization application of this product
- All data used for this assessment were directly taken from the EPAR of this product (EPAR EMA/CHMP/403683/2013 available from the EMA website)
- The value judgments provided throughout this example are hypothetical and do not reflect the opinion of the CHMP

Overview of the decision problem



Effects table



Regorafenib - Initial marketing authorization application

Overview | Effects table | Scenario Default + | Preferences | Results

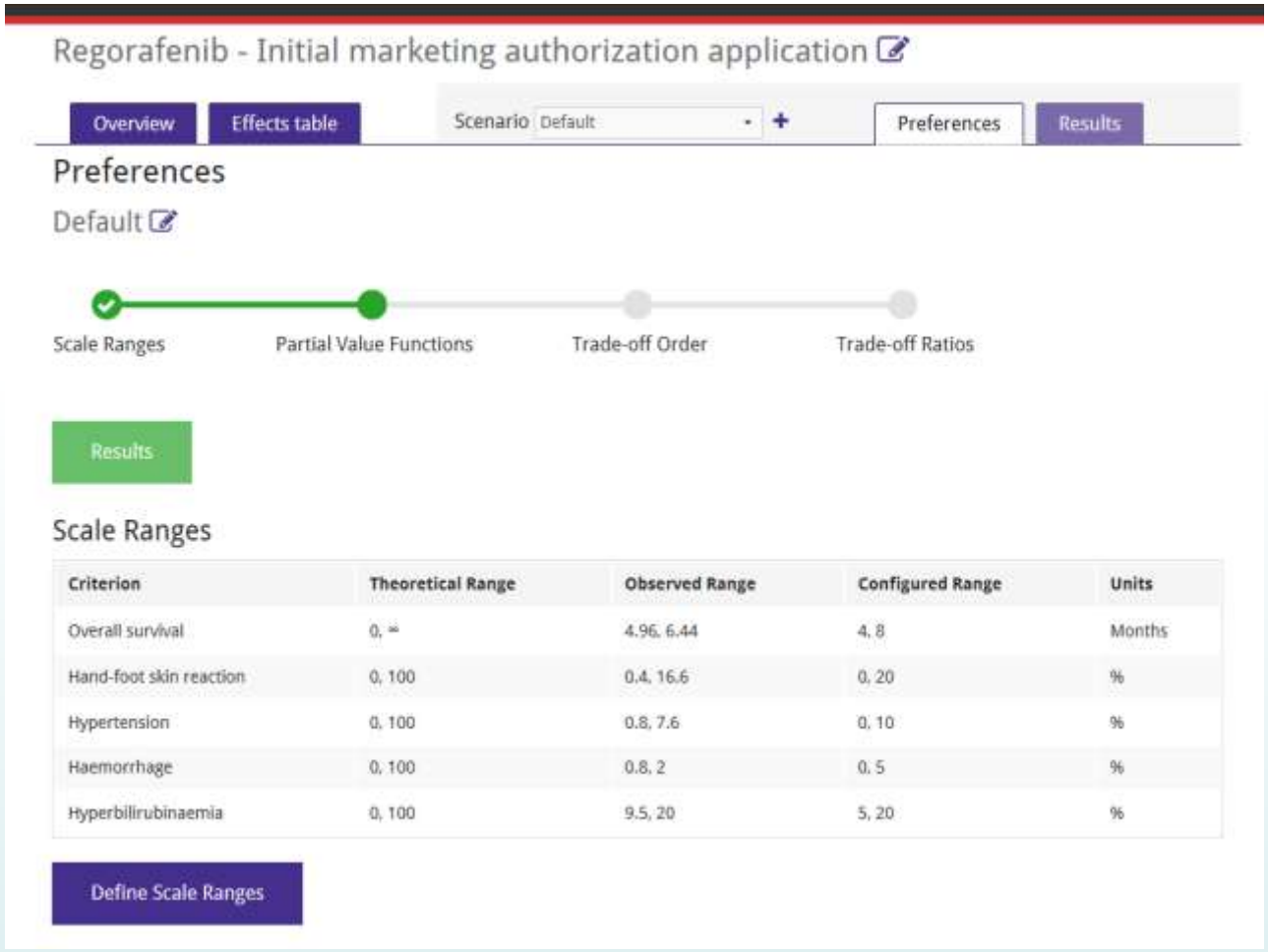
Effects table

Show alternatives

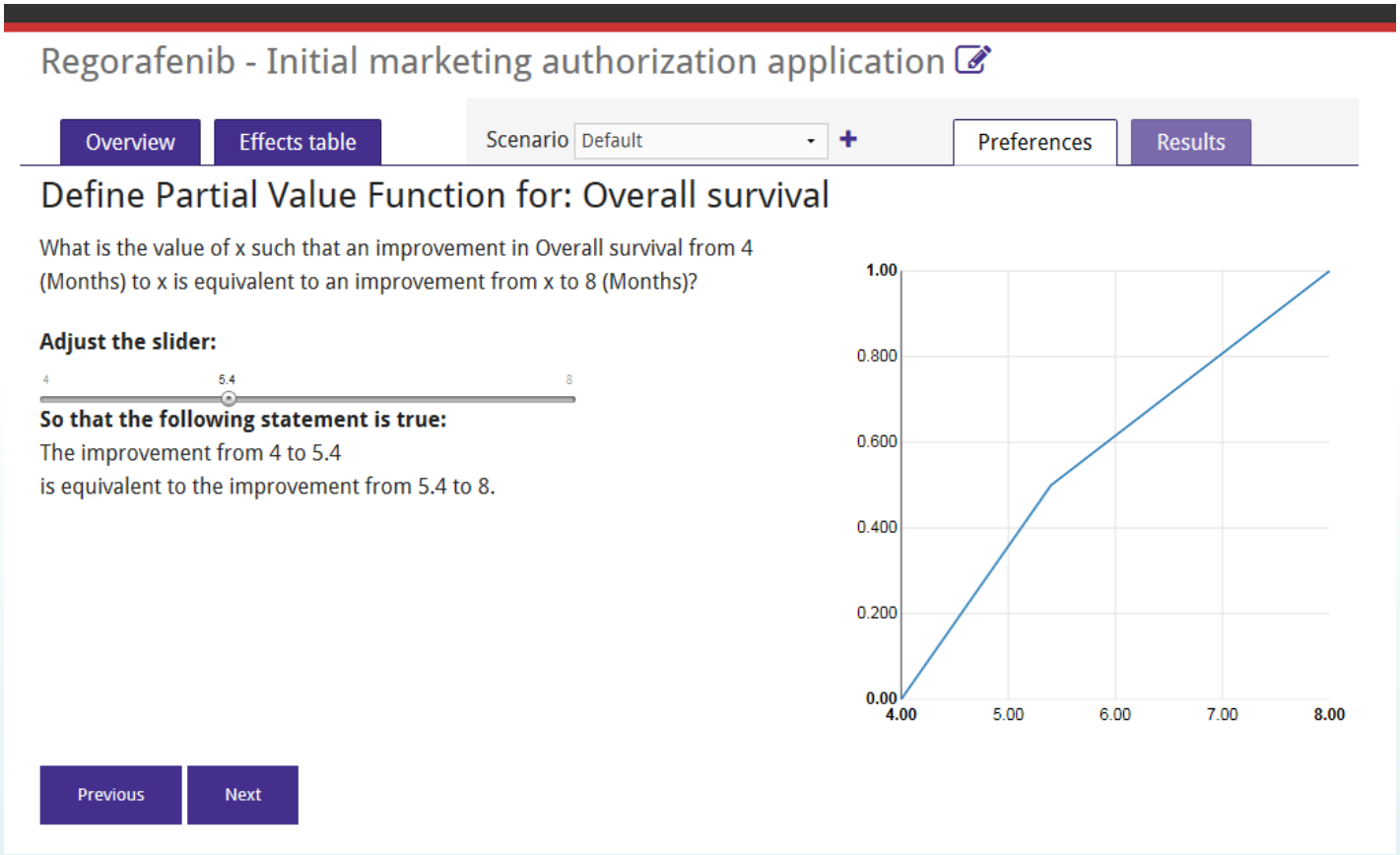
☑Placebo ☑Regorafenib

Criterion	Description	Units	Placebo	Regorafenib
Favourable effects				
Overall survival	Median overall survival time	Months	4.96 4.96, 4.96	6.44 6.44, 6.44
Unfavourable effects				
Hand-foot skin reaction	Incidence of grade 3 events	%	0.4 0.4, 0.4	16.6 16.6, 16.6
Hypertension	Incidence of grade 3 events	%	0.8 0.8, 0.8	7.6 7.6, 7.6
Haemorrhage	Incidence of grade 3-5 events	%	0.8 0.8, 0.8	2 2, 2
Hyperbilirubinaemia	Incidence	%	9.5 9.5, 9.5	20 20, 20

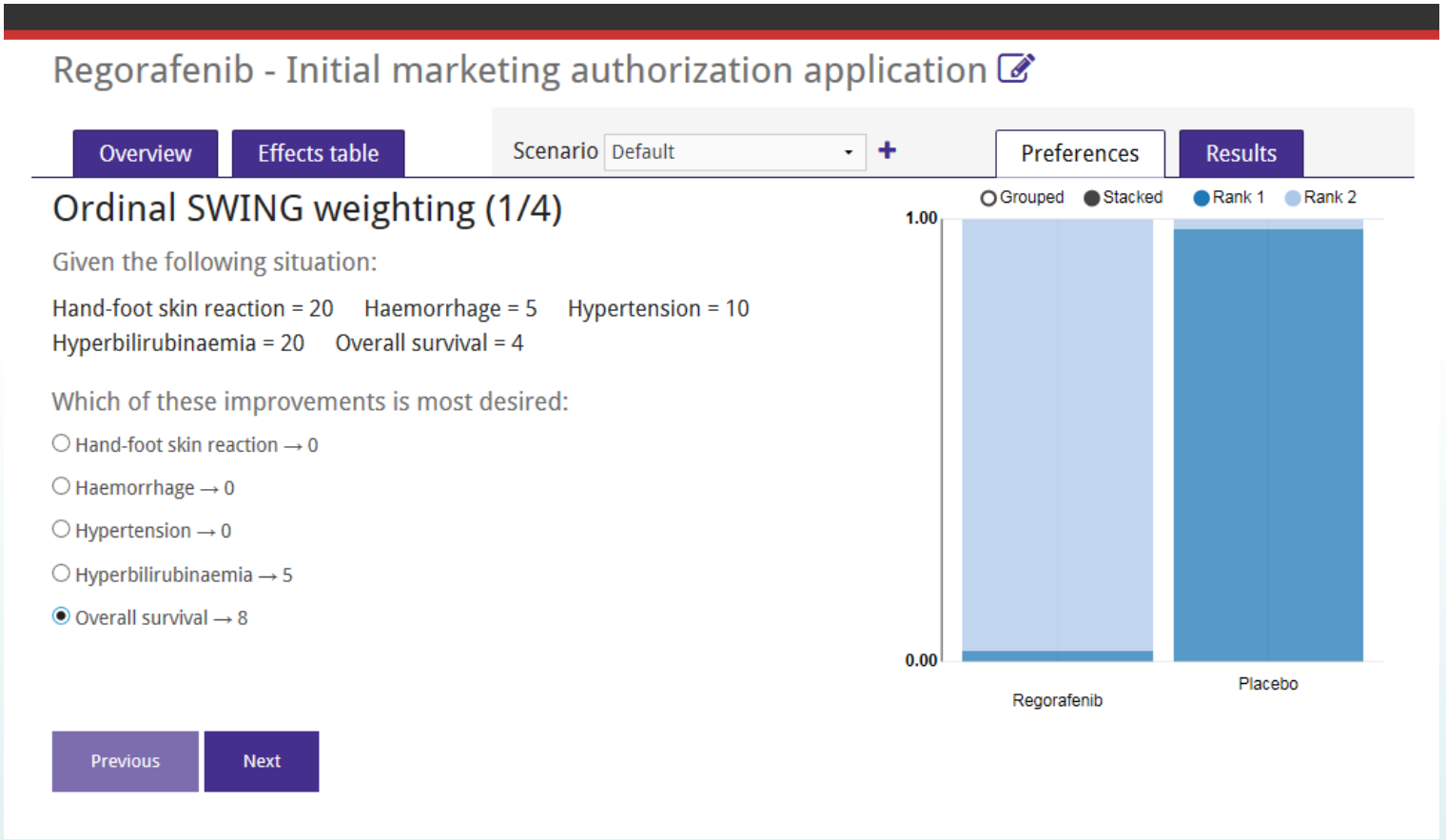
Preference elicitation: scale ranges



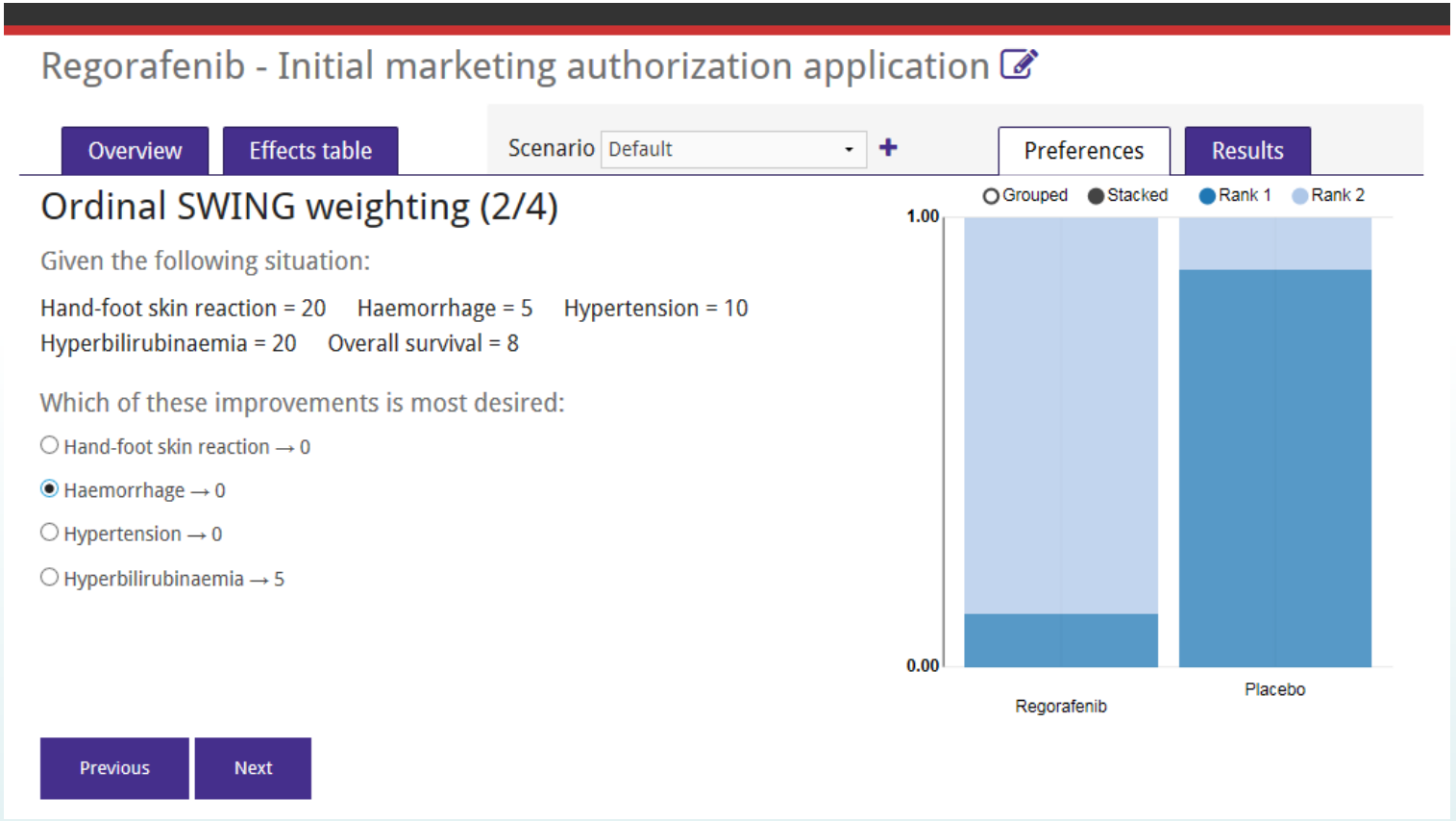
Preference elicitation: partial value functions



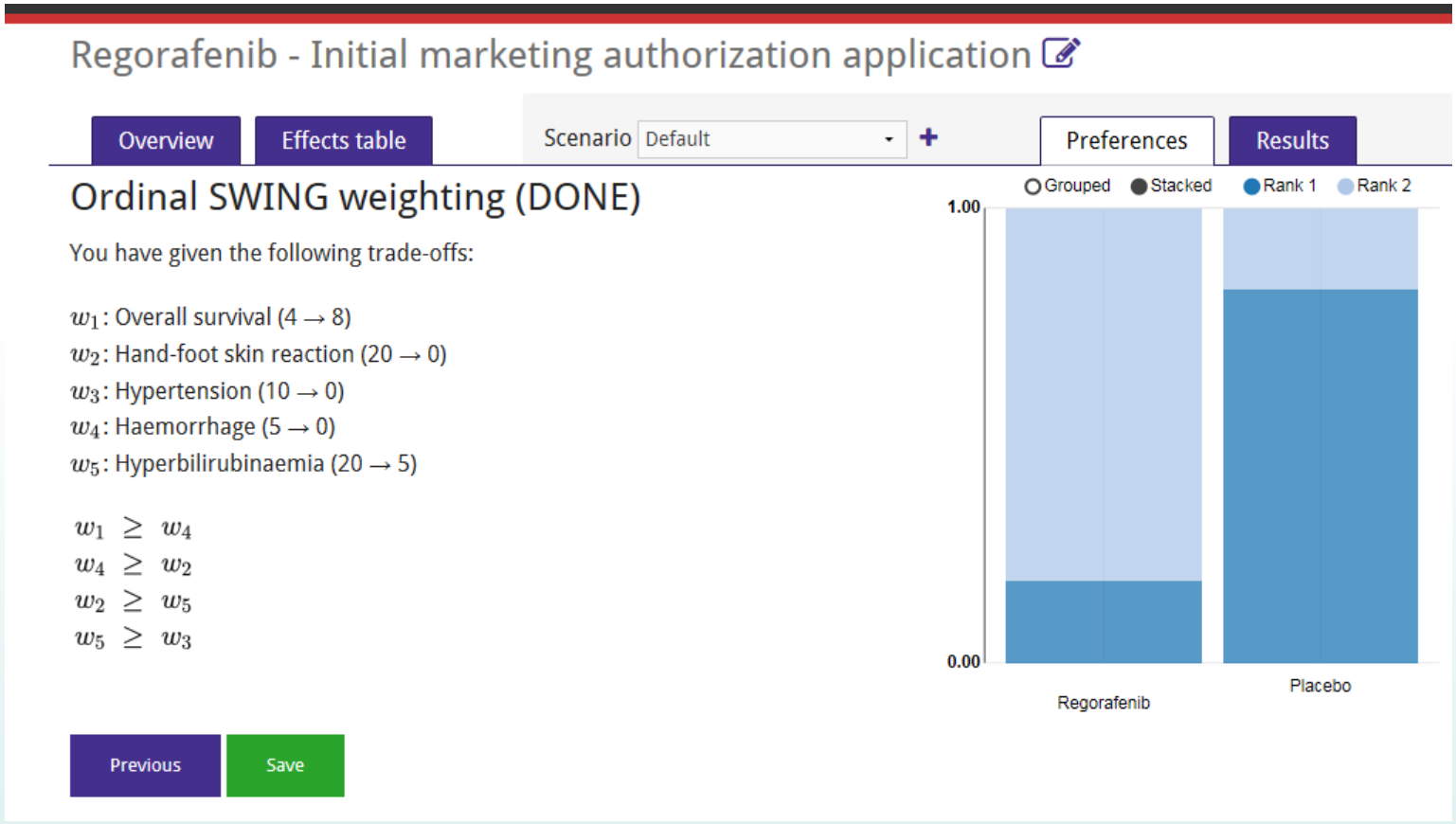
Preference elicitation: ordinal trade-offs



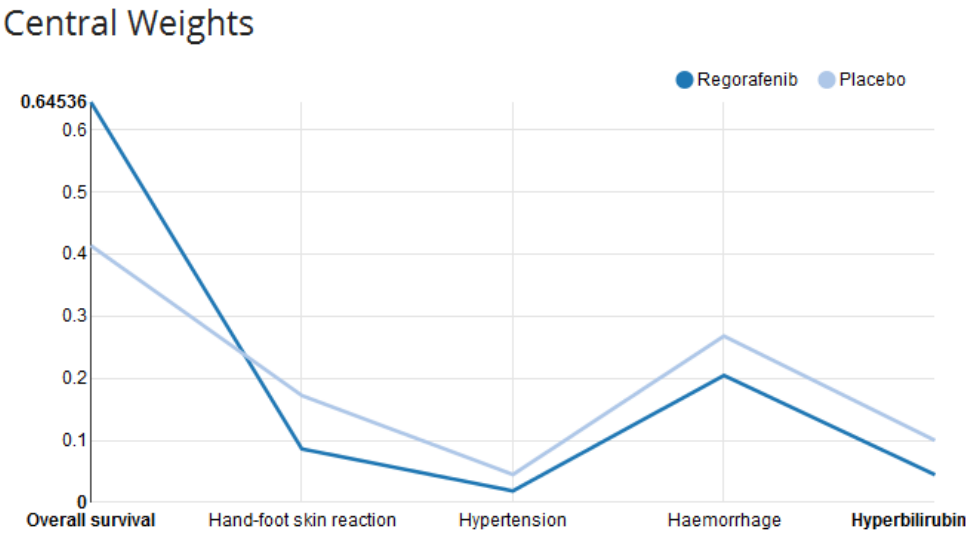
Preference elicitation: ordinal trade-offs



Preference elicitation: ordinal trade-offs

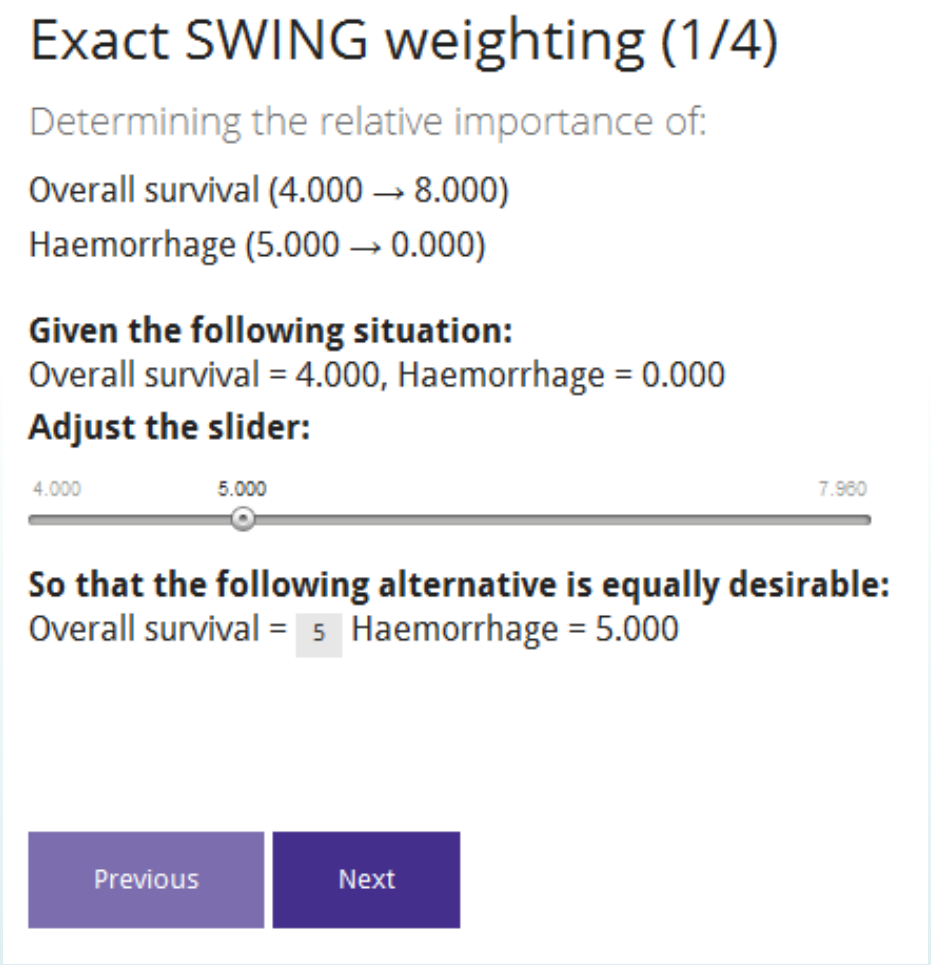


Results based on ordinal trade-offs

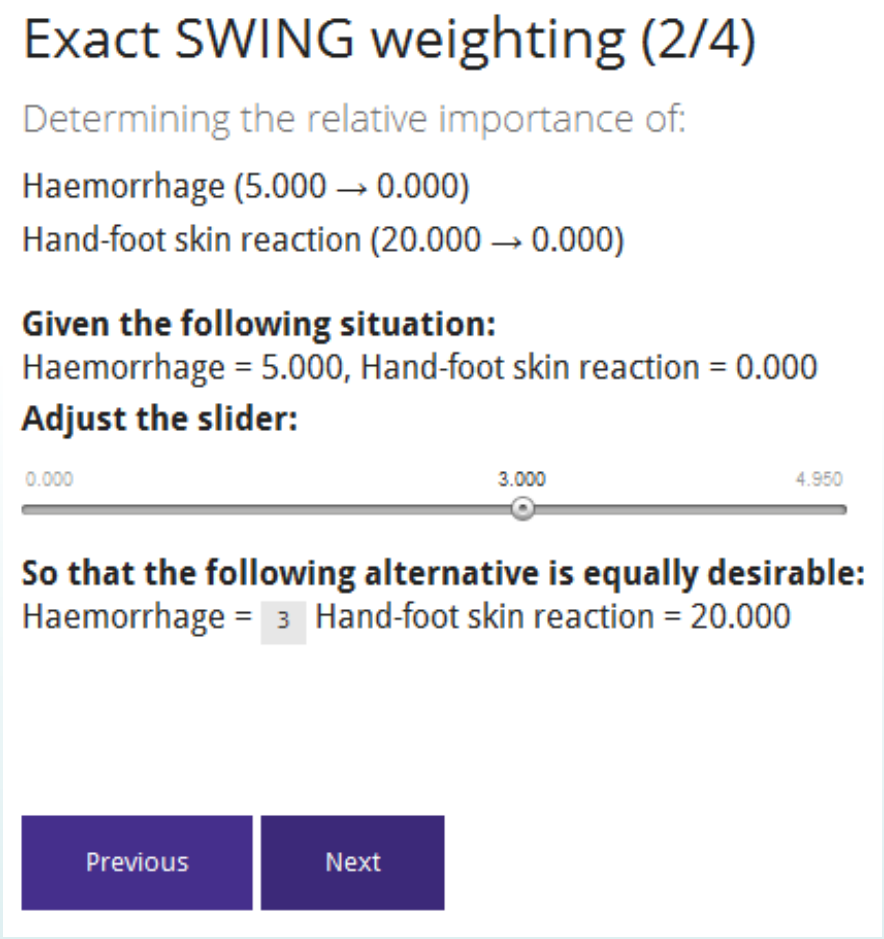


Alternative	Confidence	Hand-foot skin reaction	Haemorrhage	Hypertension	Hyperbilirubinaemia	Overall survival
Placebo	1	0.17248	0.26829	0.045044	0.10019	0.414
Regorafenib	1	0.086353	0.20483	0.018686	0.04477	0.64536

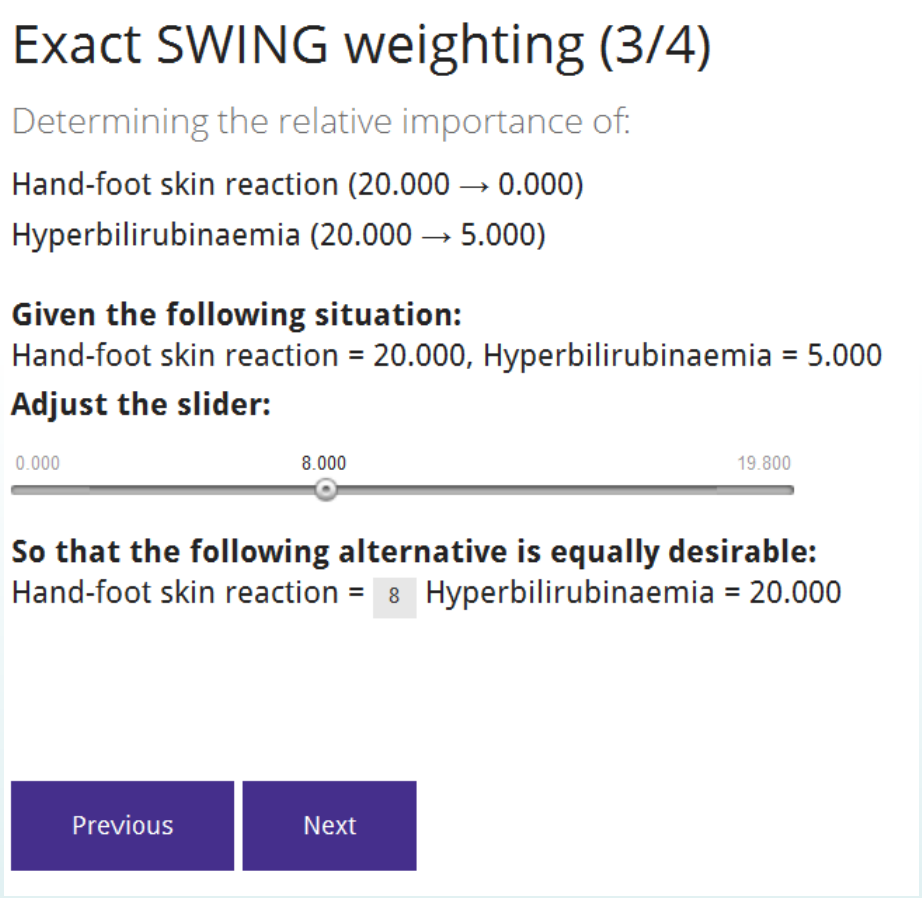
Preference elicitation: exact trade-offs



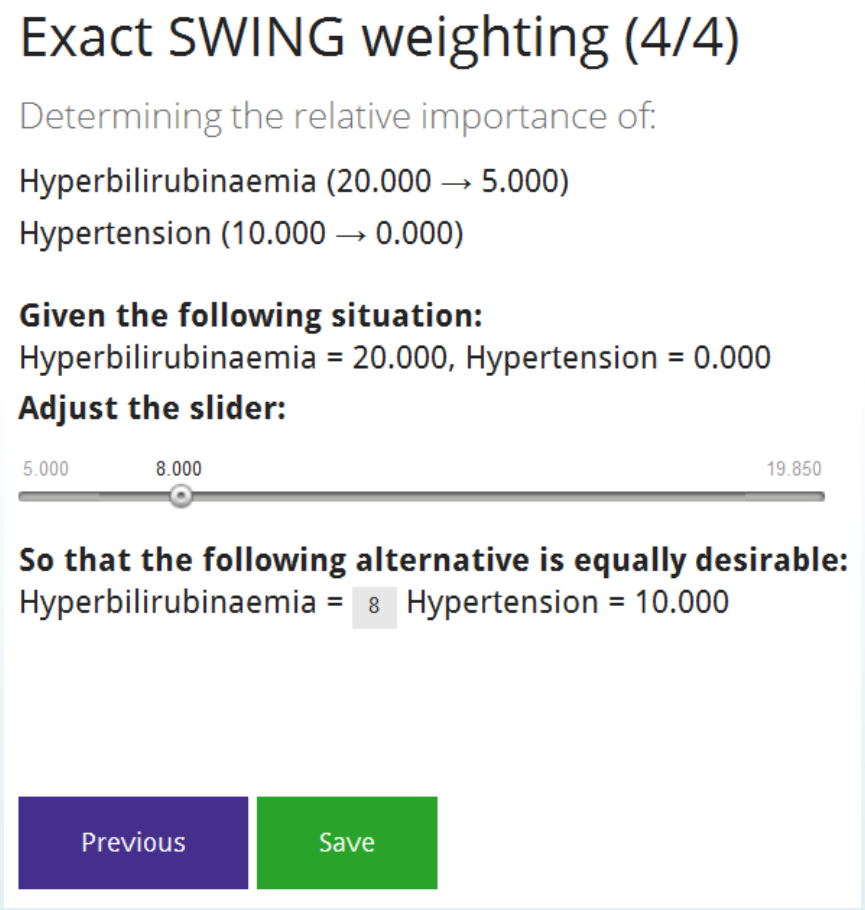
Preference elicitation: exact trade-offs



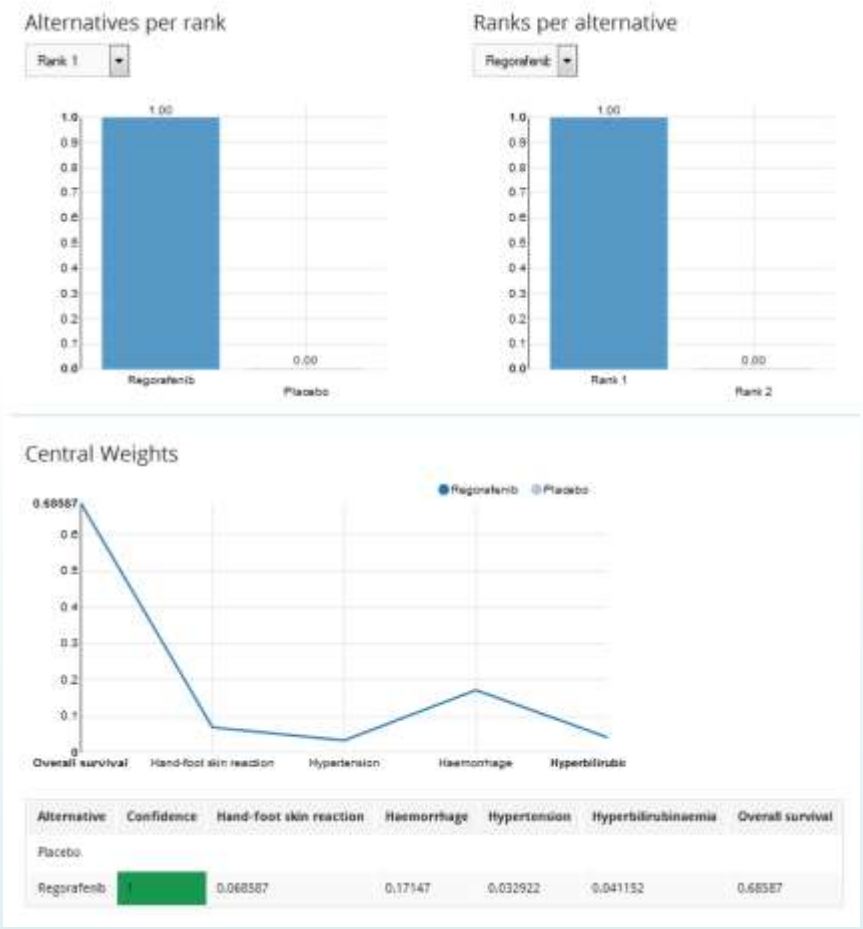
Preference elicitation: exact trade-offs



Preference elicitation: exact trade-offs



Results based on exact trade-offs



Concluding remarks

- Developing quantitative methods that are both theoretically sound and easy to use by decision makers has proven to be far from straightforward
- Our ultimate aim will be to arrive at methodologies that allow decision makers to simultaneously explore
  - Imprecision in the preference statements (i.e. shape of the partial value functions, criteria weights)
  - Uncertainty in the effect size estimates
  - Uncertainty in the long-term clinical consequences
- We have started to develop a flexible set of tools to address all these aspects (www.drugis.org)

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ADDIS

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