Continued ITI versus prophylaxis with NovoSeven® RT? An immune tolerance induction failure cost analysis model.

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OBJECTIVES

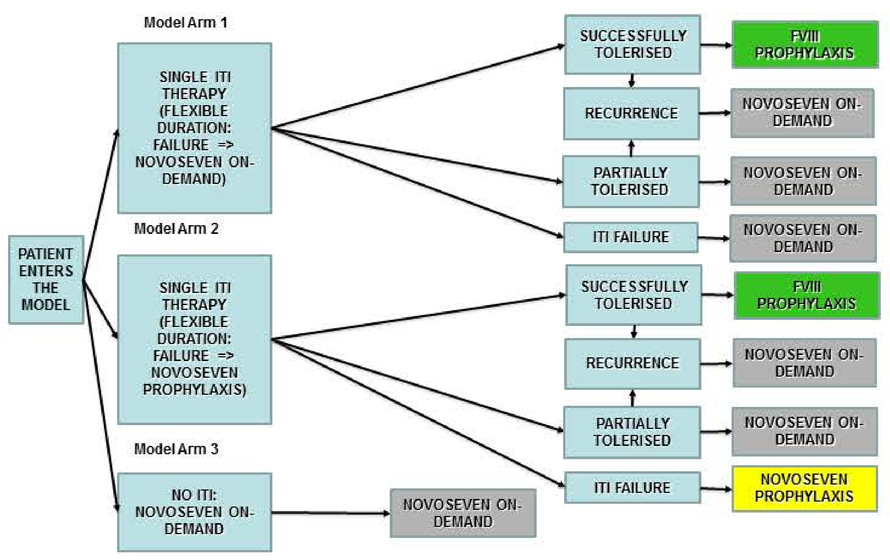
Overview: The development of inhibitors to factor VIII in patients with haemophilia A is the most important complication of modern management. Immune tolerance induction (ITI) remains the cornerstone of management and is successful in ~70% of patients. Failure of ITI is difficult to accurately define.[1]
Patients with inhibitors may also be managed with prophylaxis with bypassing agents to reduce bleeding episodes. The decision to start, or continue ITI, or to commence a patient on prophylaxis with bypassing agents, is difficult and presents significant economic challenges.

Aim: To estimate treatment costs of ITI versus using recombinant VIIa (NovoSeven® RT) using two cost analysis models:
➢A 'simple' model which compares three treatment arms (ITI followed by NovoSeven® RT on-demand, ITI followed by NovoSeven® RT prophylaxis and NovoSeven® RT on-demand alone)
➢A 'lifetime' model with multiple treatments up to 10 years ITI with user definable treatment regimens and success rates.

Here we report on the simple cost analysis model that estimates treatment costs of the three treatment arms above.

METHODS

A simple ITI costing model was developed using assumptions based on typical demographic, clinical and laboratory based inputs from real patient examples. Assumptions and inputs are user defined. The model compares costs of ITI with theoretical costs of management of the same patient with on-demand OR prophylaxis with NovoSeven® RT.



The model calculates the break-even point (BEP) = the point at which the cumulative costs of the treatment strategy (model arm 1) become equal to (or less than) the cumulative costs of the comparative treatment (model arm 2 or 3).

RESULTS

Inputs / Assumptions (all modifiable)*
*default inputs based on personal clinical experience, unless otherwise stated

•Success rates (from Hay *et al.*, 2012):
- Full Success = 69.7% ➔ FVIII prophylaxis & reduced bleeds
- Partial Success = 4.5% ➔ NovoSeven® RT on-demand (reduced dose) and reduced bleeds
- Failure = 25.8% ➔ NovoSeven® RT on-demand & no change in bleed rates
  No ITI: NovoSeven ® RT on-demand

•Recurrence rates (default inputs based on Antun *et al.*, 2013 clinical experience)
- Fully tolerised (30%), recurrence after 3 years.
- Partially tolerised (50%), recurrent after 2 years.

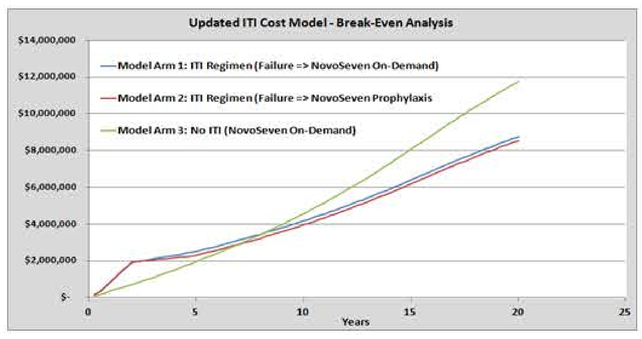
•Health states used to define the treatment received and risk of events
- Bleed events are categorised as typical bleed or severe bleed
- Severe bleeds are assumed to be bleeds that require hospitalisation and significantly higher on-demand dose
- Bleed rates (annual frequency)
  - ITI full success = 5 typical, 0.5 severe.
  - ITI failure= 72 typical, 4 severe.
  - NovoSeven® RT = 4 typical, 1 severe.

•Hospitalisation:
- Required for 'Severe Bleed' (AR-DRG Cost per event = $2,845 AR-DRG Average Length of Stay = 2.53)

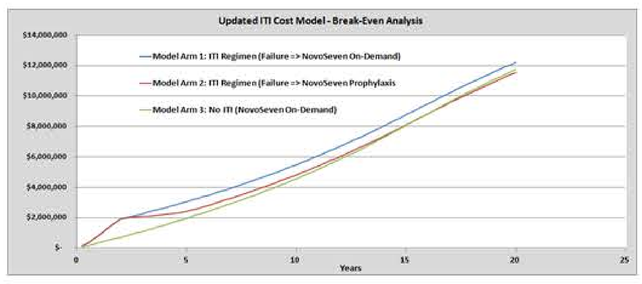
•Adverse events: (default inputs based on Hay *et al.*, 2012 & clinical experience)
- Potential for IV-Line infection for FVIII-treated patients, no AE's for patients receiving NovoSeven® RT;
- Rate used = 1 infection per patient, per year; 25% chance of an infection during each 3 month cycle while receiving ITI therapy with FVIII; Cost per adverse event = $11,971).

RESULTS

Cumulative costs and BEP for ITI regimens vs NovoSeven® RT On-Demand

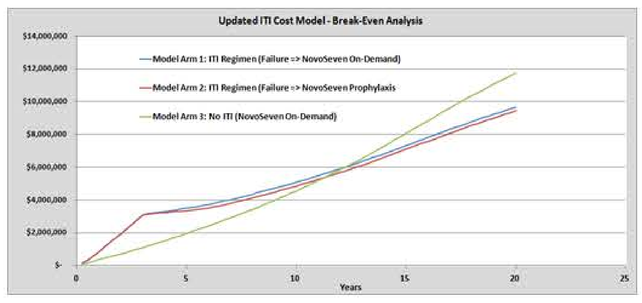


BASE CASE
•Arm 1 v Arm 3 BEP = 8.25 years
•Arm 2 v Arm 3 = 7.2 years
•Prophylaxis NovoSeven® RT (Arm 2) is slightly less costly than Arm 1, due to the temporary reduction in bleeds as a result of the prophylaxis use.
•NovoSeven® RT prophylaxis is received by only ~26% of patients in the base case (i.e. only patients who failed ITI therapy).



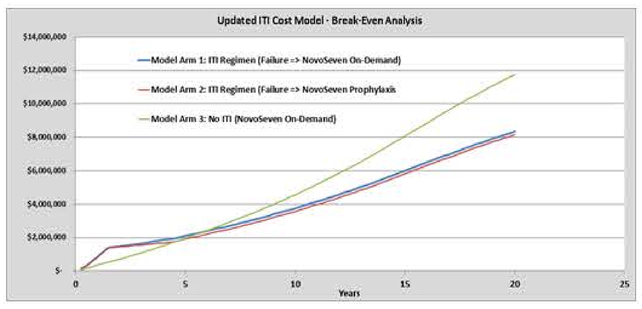
DECREASED PROBABILITY ITI SUCCESS (69.7% to 15%)
Arm 1 v Arm 3 = >20 years
Arm 2 v Arm 3 = 16 years

"Assuming a 15% probability of success the costs of ITI therapy are unlikely to be recouped within 20 years "



LONGER DURATION ITI (2 TO 3 YEARS)
Arm 1 v Arm 3 = 12.25 years
Arm 2 v Arm 3 = 11.5 years

"Assuming a 3-year duration of ITI costs of ITI therapy will be re-couped in 11.5-12.25 years"



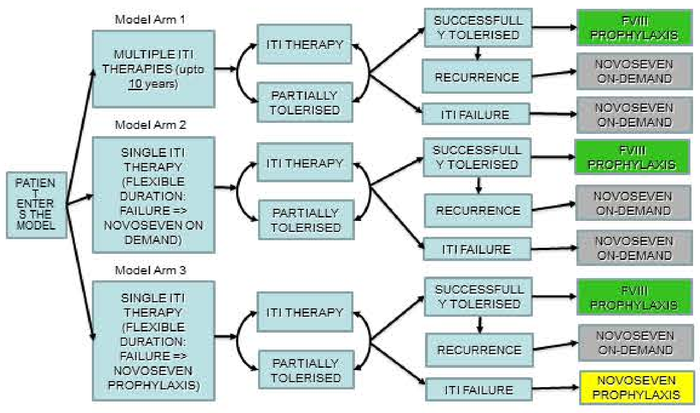
SHORTER DURATION ITI (2 TO 1.5 YEARS)
Arm 1 v Arm 3 = 6 years
Arm 2 v Arm 3 = 4.75 years

"Assuming a 1.5-year duration of ITI costs of ITI therapy will be re-couped in 4.75 to 6 years"

ITI is the preferred management strategy for patients with haemophilia A who develop high titre inhibitors to factor VIII. Unfortunately, not all patients who commence ITI will have successful immune tolerance. There is little information available about costs of different treatment approaches.
This cost model offers information on different treatment regimes. The model suggests that in patients with a high chance of success the decision to start ITI is economically rational with the high up-front costs of ITI recouped within 5-10 years. In contrast, patients who have a reduced rate of success (e.g. <20% success rate) there is a large clinical cost burden of ITI that is unlikely to be recouped.

DISCUSSION & FUTURE DIRECTIONS

A 'lifetime' model with multiple treatments up to 10 years ITI with user definable treatment regimens and success rates is under development.
A summary schematic is shown here.



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2. Hay CR, DiMichele DM (On behalf of the ITI Study Group). The principal results of the International Immune Tolerance Study: a randomized dose comparison. Blood. 2012 Feb 9;119(6):1335-44
3. Antun et al. Poster1106 Natural History Of Inhibitor Recurrence Following Successful Immune Tolerance Induction. 55th Annual ASH meeting, 2013. *unpublished data*

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