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The Optimized Patient Treatment Initiative (OPT-In): Choosing the Right Therapy, for the Right Patient, at the Right Time

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Background

- The full landscape of immune-mediated disorders includes gastrointestinal, dermatological and rheumatological diseases. Patients with these chronic conditions require treatment for prolonged periods of their life and finding effective treatments during the course of their disease can be challenging
- Whilst multiple new and effective treatment options have attained marketing authorization by the European Medicines Agency (EMA), uncertainty remains around the optimal order of treatments – and, crucially, which treatment should be used first. Despite the many advanced options available, patients often start therapy with less-effective or cheaper treatments due to national and/or local prescribing restrictions informed primarily by budget considerations
- The Optimized Patient Treatment Initiative (OPT-In) model was developed to determine the likely optimal sequences of treatment and inform decision making, with the aim of demonstrating that by adopting a 'best treatment first' prescribing policy instead of a 'cheapest treatment first' policy, a sustainable healthcare system and improved patient outcomes can be achieved
- Italy was selected as the country to demonstrate the functionality and potential of OPT-In because, in addition to the initial national level reimbursement assessment carried out by the Italian Medicines Agency (AIFA), Italy has 20 regions, each with the authority to apply the reimbursement decision by AIFA in line with their respective needs and constraints. This can result in regional variation in treatment access and therefore is an ideal setting in which to assess the impact of a 'best treatment first' policy versus a 'cheapest treatment first' policy. Additionally, Italy has a historically high incidence of plaque psoriasis (PsO). PsO can therefore be assessed with deeper consideration in the Italian setting and lends itself as helpful to demonstrate the impact of OPT-In

Objective: To investigate how choosing 'best treatment first' prescribing policies instead of 'cheapest treatment first' policies affects patient outcomes and healthcare system sustainability, using OPT-In.

Methods

Model structure

- The OPT-In model is a state-transition model that was developed to assess the efficacy of treatment sequences in seven immune-mediated disorders: Crohn's disease (CD), ulcerative colitis (UC), PsO, psoriatic arthritis (PsA), rheumatoid arthritis (RA), ankylosing spondylitis (AS) and non-radiographical axial spondylarthritis (NR-AxSpA)
- In accordance with previous modelling in immunology, each treatment line is defined by two treatment phases: induction and maintenance. For treatments that do not require an induction period, the maintenance phase starts from initiation of treatment. All treatments with EMA marketing authorization at the end of 2020 were included
- The model used a 3-year time horizon, with 2021 as the start year

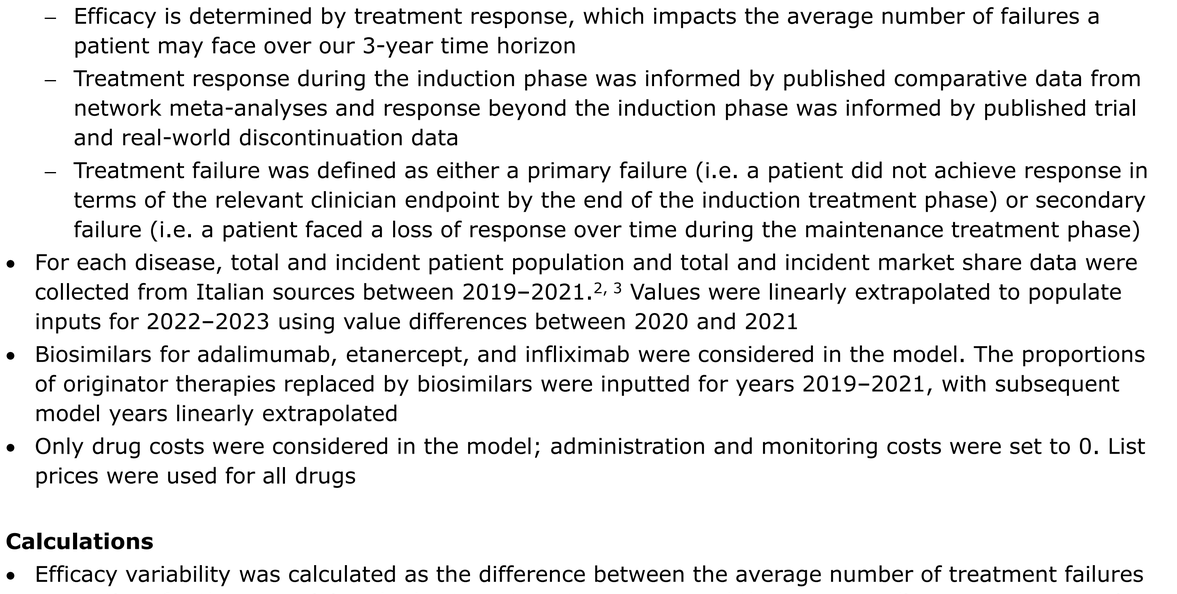
Data inputs and assumptions

- All efficacy inputs, calculations and assumptions used by the OPT-In model are presented in detail by Boer et al.[1]
  - Efficacy is determined by treatment response, which impacts the average number of failures a patient may face over our 3-year time horizon
  - Treatment response during the induction phase was informed by published comparative data from network meta-analyses and response beyond the induction phase was informed by published trial and real-world discontinuation data
  - Treatment failure was defined as either a primary failure (i.e. a patient did not achieve response in terms of the relevant clinician endpoint by the end of the induction treatment phase) or secondary failure (i.e. a patient faced a loss of response over time during the maintenance treatment phase)
- For each disease, total and incident patient population and total and incident market share data were collected from Italian sources between 2019–2021.[2, 3] Values were linearly extrapolated to populate inputs for 2022–2023 using value differences between 2020 and 2021
- Biosimilars for adalimumab, etanercept, and infliximab were considered in the model. The proportions of originator therapies replaced by biosimilars were inputted for years 2019–2021, with subsequent model years linearly extrapolated
- Only drug costs were considered in the model; administration and monitoring costs were set to 0. List prices were used for all drugs

Calculations

- Efficacy variability was calculated as the difference between the average number of treatment failures per patient for those receiving the best treatment sequence and the corresponding average per patient of those receiving the worst treatment sequence within the time horizon
- The efficacy of 'top sequences' was calculated by ordering sequences by number of treatment failures and weighting the top 20% of sequences equally. Weighting the top 20% of sequences was considered important as it was acknowledged that patient needs will vary and therefore, one single sequence would never be prescribed for all

Figure 1: Efficacy variation across seven immune-mediated disorders



Key: AS, ankylosing spondylitis; CD, Crohn's disease; NR-AxSpA, non-radiographical axial spondylarthritis (NR-AxSpA; PsA, psoriatic arthritis; PsO, plaque psoriasis; RA, rheumatoid arthritis; UC, ulcerative colitis.

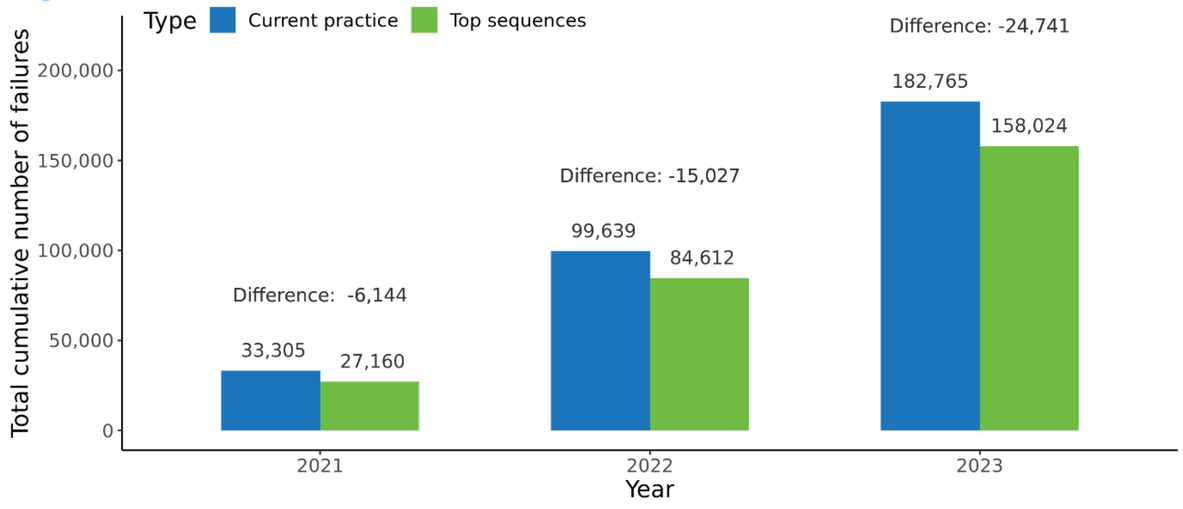
- Current practice efficacy was estimated using the Italian incident market share data; treatment failure outcomes of sequences with the same incident therapy were averaged then weighted according to incident market shares
- Overall costs were estimated by using the incident and prevalent market shares to estimate costs per year for each patient and for each disease. These were then multiplied by the relevant number of incident and prevalent patients provided by Italian inputs

Results

Efficacy

- In **Figure 1**, the variation in efficacy between treatment sequences is displayed. The green portion of the bars show the sequences that are most efficacious (i.e. fewer treatment failures) while the red/orange portion shows the sequences that are least efficacious. The difference between the top and bottom of the bars represents all of the possible sequences and their related efficacy. The blue triangles capture the average national prescribing behaviour in Italy relative to all the available treatment sequences. The 'gap' between the blue triangle and the green portion of the bar represents the opportunity for improvements in prescribing – a larger gap indicates a greater opportunity for improvement
- In PsO, 1,284 treatment sequences are possible. The estimated average number of failures ranges from 0.58 to 2.44 over 3 years; the most prescribed sequences result in an average of 1.14 failures, suggesting possible improvements
- If improvements were implemented, treatment failures could be reduced by up to 0.56 in PsO over 3 years and 0.25 in UC, 0.23 in PsA, 0.23 in RA, 0.16 in CD, 0.12 in AS, and 0.10 in NR-AxSpA

Figure 2: Estimated total number of treatment failures



- **In all diseases, the most efficacious sequence had the most efficacious available individual therapy prescribed in the first line of treatment.** Likewise, the top pool of the 20% most efficacious sequences trended towards patients receiving more efficacious therapies earlier in the treatment pathway

Implementation

- A scenario was explored where all sequences were ordered by average number of treatment failures, and only the top 20% most-efficacious sequences were used. This was called the 'top sequences' scenario and was compared with the estimated current practice in Italy
- Across all seven indications, it was estimated that implementing the top sequences scenario over current practice would prevent a total of 24,741 treatment failures across the 3-year time horizon (**Figure 2**), a decrease of 13.5%
- **Table 1** shows the cumulative cost of each disease over the 3-year time horizon for the current practice; alongside this, the impact of implementing the top sequences scenario are presented
  - Where prescribing practice shifts such that only the top sequences are prescribed, the budget changes vary between +12.9% in UC and -2.7% in RA, with an overall increase of +4.78% across all diseases
  - As OPT-In acknowledges that there is a place in therapy for all treatments, it was important to consider the impact of biosimilar anti-tumour necrosis factors (TNFs) displacing their originators; therefore, when this biosimilar uptake was also considered, the cost of implementing the top sequences is offset to varying degrees for all diseases. The overall 3 year spending impact in this scenario is +3.48%

Table 1: Cumulative cost of implementation over 3-year time horizon

Disease Name	Current practice (€)	Top sequences impact (€)	Biosimilar impact (€)	Total cost (€)	Cost difference with top sequences and biosimilar impact
CD	580,854,325	42,959,977	-8,816,780	614,997,522	5.88%
UC	420,391,679	54,288,539	-4,065,373	470,614,845	11.95%
PsA	718,881,890	56,680,929	-11,259,851	764,302,968	6.32%
RA	1,051,722,148	-28,833,358	-11,698,657	1,011,190,133	-3.85%
PsO	908,839,395	36,298,653	-3,061,624	942,076,424	3.66%
AS	369,382,136	32,511,965	-8,977,119	392,916,982	6.37%
NR-AxSpA	344,538,008	16,003,321	-8,941,842	351,599,487	2.05%
Total costs:	**4,394,609,581**	**209,910,025**	**-56,821,245**	**4,547,698,362**	**3.48%**

Strengths and Limitations

- Key strengths of this analysis include being the first known model that considers a holistic view of the full immunology space, acknowledging that there is an appropriate place in therapy for all classes of treatment, whilst considering that patient needs vary so physicians require choice; therefore, the implementation of 'best treatment first' considers top 20% of the most efficacious sequences and not just the single most efficacious. Finally, additional benefits of performing the analyses in an R application include the accessibility and security of an online web deployment and scalability for adapting across numerous localities
- Key limitations of this analysis include the lack of market share and efficacy inputs for modelling subsequent treatment lines conditional on specific induction therapy. The external validity of the model could be improved by the addition of more real-world evidence studies to these inputs

Conclusions

- The model results suggest that the disease areas with the greatest opportunity for efficacy improvement in Italian patients through shifts in prescribing practice were PsO, UC, PsA and RA
- The results further suggest that the use of the top 20% most efficacious sequences would result in a 13.5% improvement in patient outcomes and a 3.48% budget increase
- In all diseases, the most efficacious sequences trended towards using the most efficacious individual therapies in the first instance (i.e. in first line of therapy). These results therefore support 'best treatment first' prescribing policies in Italy
- The use of the OPT-In model demonstrated the benefits and costs of implementing more efficacious prescribing practices in an Italian setting and suggests that this shift in prescribing policy could provide the greatest opportunity to reduce treatment failures, maximize patient outcomes, and promote a sustainable healthcare system

Disclosures

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1. Boer J, Hassan F, Alulis S, et al. Analysis of Treatment Sequences across Seven Immunological Diseases and the Variability in Efficacy for Patients per Disease: Opportunities for Improvement. Virtual ISPOR Europe 2021. 30 November - 3 December 2021. POSC319.
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