COST PER RESPONDER ANALYSIS EVALUATED THROUGH CLINICAL RESPONSE AND REMISSION RATE OF ADALIMUMAB, USTEKINUMAB AND VEDOLIZUMAB FOR THE TREATMENT OF CROHN'S DISEASE FROM THE BRAZILIAN PRIVATE HEALTHCARE SYSTEM PERSPECTIVE

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INTRODUCTION:

Crohn's disease (CD) is a complex, chronic inflammatory disorder that is associated with potentially debilitating physical symptoms, which in turn can have a substantial impact on patients' overall well-being and quality of life.[1]

A Brazilian study found a prevalence ratio of 5.65 cases and an incidence ratio of 3.50 cases in 100.000 inhabitants between 2001 and 2005[2]. Although CD is not as prevalent as some other chronic diseases, its impact on patients' lives is extensive.[1]

Given the disease chronicity, long disease duration, frequent early adult onset, and the need for hospitalization or surgery, poorly managed CD can lead to substantial costs.[3] The treatment goal for patients with CD is therefore to achieve long-term remission, which provides a number of benefits for patients, their families, care providers and employers.[4]

OBJECTIVES:

The aim of this study is to compare cost per patient achieving clinical response and cost per patient in clinical remission of adalimumab (ADA), ustekinumab (UST) and vedolizumab (VEDO) for the treatment of Crohn's disease (CD) from the Brazilian private payer perspective.

METHODS:

Clinical response

Clinical response was evaluated through CD activity index reduction of 100 points (CDAI-100) and remission rate was evaluated through CD activity index score under 150 points (CDAI<150) in overall patients with CD.

To compare ADA, UST and VEDO clinical outcomes, a network metanalysis published4 in 2019 was accessed. Infliximab and certolizumab were not included in the analysis due to lack of data in this metanalysis. The clinical response and remission rate from the network metanalysis are shown in Table 1.

Table 1: Clinical response and remission rate (odds ratio)[4]

			Dose escalation	
Drug	**CDAI-100**	**CDAI<150**	**CDAI-100**	**CDAI<150**
Adalimumab	1,42	1,34	1,37	1,29
Vedolizumab	1,61	1,6	1,58	1,55
Ustekinumab	1,01	1,03	NA	NA

Costs

Only drug acquisition costs were considered, which was obtained on official price magazine (Table 2), and calculated according to label. The approved posology and number of doses per year for each drug are shown in Tables 3 and 4, respectively.

Table 2: Drug acquisition costs

Drug	Price (PF18%)[5]
Adalimumab 40mg (2 syringes)	BRL 8,016.61
Ustekinumab 90mg	BRL 25,161.87
Vedolizumab 300mg	BRL 14,525.26

Table 3: Number of doses per year

Drug	Induction	Maintenance	Maintenance with dose escalation
Adalimumab[6]	30	26	52
Vedolizumab[7]	8	6,5	13
Ustekinumab[8]	7	4,3	6,5

Table 4: Posology of Crohn's disease treatment according to approved label

Drug	Standard posology	Adjusted posology (dose escalation)
Adalimumab[6]	160mg at week 0.80mg at week 2. From week 4, 40mg every 14 days.	40mg every week.
Ustekinumab[7]	First dose: 260-520mg IV. At week 8, 90mg SC, then 90mg SC every 12 weeks.	90mg SC every 8 weeks.
Vedolizumab[8]	300mg at week 0, 2 and 6, then 300 mg every 6 weeks.	300mg every 4 weeks.

Cost per patient achieving clinical response and cost per remittent patient were calculated through the ratio of induction and maintenance year costs by the proportion of patients achieving CDAI-100 and CDAI<150, respectively.

In the analysis with dose escalated clinical data, costs were calculated accordingly.

For a three-years time horizon hypothetical scenario, clinical data was considered the same, but costs calculated accordingly. This time horizon was based on the potential beneficiary turnover among health plans.

RESULTS:

The proportion of patients achieving CDAI-100 and CDAI<150 found on literature and applied in this analysis is described in table 5.

Table 5: Proportion of patients achieving CDAI-100 and CDAI<150 according the literature

			Dose escalation	
Drug	**CDAI-100**	**CDAI<150**	**CDAI-100**	**CDAI<150**
Adalimumab	22%	21%	23%	22%
Vedolizumab	19%	18%	20%	18%
Ustekinumab	31%	27%	31%	28%

Cost per patient achieving clinical response (CDAI-100)

The cost per achieving clinical response on induction year was similar between the treatments, with ADA treatment presenting a slightly lower cost per patient achieving clinical response compared to UST and VEDO; When considered maintenance, maintenance with dose escalation and 3-year scenario, UST was the treatment with the lowest cost per biologic naïve patient achieving clinical response in all scenarios (Figure 1).

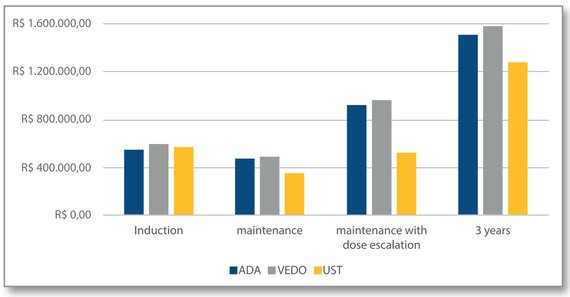

Figure 1. Cost per biologic naïve patient achieving clinical response comparison

Cost per patient in clinical remission (CDAI<150)

The cost per patient in clinical remission on induction year was also similar between the treatments, with ADA presenting a slightly lower cost per remitter patient on induction year compared to VEDO and UST; When considered maintenance, maintenance with dose escalation and 3-year scenario, UST was the treatment that presented the lowest cost per biologic naïve remitter patient in all scenarios (Figure 2).

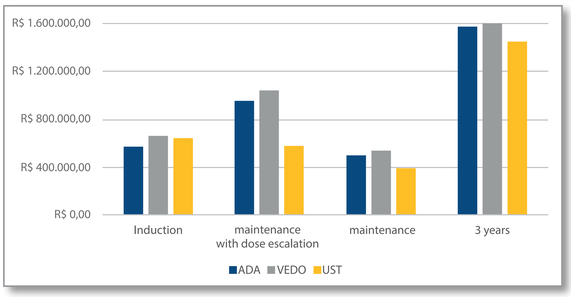

Figure 2. Cost per patient in clinical remission comparison

DISCUSSION:

In both the cost of maintenance analysis and the 3-year scenario, UST proved to be the lowest cost-per-response drug compared to ADA and VEDO. Considering induction year treatment, ADA represented a slightly lower cost per patient achieving clinical response and cost per remitter followed by UST and VEDO.

When maintenance with dose escalation treatment is estimated, UST presented the lowest cost per patient achieving clinical response and cost per remitter compared to VEDO (-45.2% and -25.7%, respectively) and ADA (-42.7% and -19.6%, respectively).

As mentioned before, infliximab and certolizumab pegol were not evaluated, given they do not have sufficient data available in the network metanalysis.

Since there is no a specific time on the treatment to increase dosage, and it depends on each individual patient response, the extrapolation of one complete maintenance year with increased costs is recognized as a limitation of this study.

CONCLUSIONS:

Ustekinumab demonstrated to have a better cost per responder in scenarios of maintenance year costs, dose escalation data and three years time-horizon. Adalimumab showed to have a slightly favorable cost per responder results only in the induction year. Considering the chronic and progressive characteristic of Crohn's disease, three years time-horizon should be regarded as the most significant result in the analysis, once brings the cost per response for a more realistic period for payers.

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