PCN7

Jommi C[1], Ravasio R[2], Friggi E[3]

The value of obinutuzumab for untreated advanced follicular lymphoma: an assessment based on Multicriteria Decision Analysis (MCDA)

[1]Centre for Research on Health and Social Care Management (CERGAS), SDA Bocconi University, Milan, Italy [2]Health Publishing and Services Srl, Piazza Duca d'Aosta 12, 20124 Milano [3]Roche S.p.A., Monza, Italy

Objective

- Multicriteria decision analysis (MCDA) provides a framework that enhances transparency and repeatability of decisions taken on a multicriteria basis.
- The objective of this study was to use MCDA to obtain preferences and views on decision criteria across three stakeholder groups: patients, clinicians and payers
- This analysis assessed obinutuzumab compared to rituximab used as a first line treatment advanced Follicular Lymphoma (FL) in the Italian national health care service, using an MCDA approach based on six domains: quality of evidence, unmet need, type of benefit provided, incremental benefit/risk, incremental costs and feasibility.

Methods

- We used the EVIDEM V10 MCDA framework[1] and a Delphi[2] approach to scrutinize the views of a panel of physicians, payers and patients on value domains and their application to research target.
- The panel was composed by 5 physicians hematologists, 5 regional payers and 4 FL patients.
- Panelist were interviewed on six domains: unmet need, type of benefit provided, quality of evidence, incremental risk/benefit ratio, incremental cost and feasibility.
- It was required to provide:
  - An opinion on which domains are priority in assessing a new drug/indication in term of access, reimbursement and prescription;
  - A absolute ranking (values from 0 [minimum] to +5 [maximum]) on not comparative domains such as unmet need, type of benefit provided and quality of evidence;
  - A comparative ranking (values from -5 [maximum worsening compared to rituximab] and +5 [maximum improvement compared to rituximab]) on comparative domains such as incremental risk/benefit ratio, incremental cost and feasibility.
- Since obinutuzumab was not reimbursed as a first line treatment in advanced FL at the time of the analysis, in term of price we used a treatment cost range between a maximum value, namely obinutuzumab ex-factory price at the time of analysis, and a minimum value equal to the ex-factory price of rituximab originator.

Unmeet need *depends on (i) disease severity (a disease is as serious as it is more deadly and/or impacts on patients quality of life), (ii) from how unsatisfied this need is based on existing therapeutic alternatives on the market and (iii) the number of patients.*
Type of benefit provided *assess whether the drug can cure, slow down the progression of the disease or only have an effect on symptoms.*
Quality of evidence *refers to the type of studies carried out. For example, randomized controlled trials are considered to be of higher quality than those in which patients are not randomly assigned to an experimental arm and a control arm. The analyzes of the effects of a drug on subpopulations are considered of higher quality if planned before conducting the experimental study than those carried out subsequently (so-called "post hoc" analysis). The Evidem approach does not use any specific tool to assess the quality of the studies.*
Incremental risk/benefit ratio *evaluates, with respect to the best therapeutic alternative on the market, (i) the improvement of clinical data (increased survival and other clinical parameters that measure the effectiveness of a drug) and the quality of life of the patients and (ii) the increase number and severity of side effects.*
Incremental cost *means an increase in the unit cost per patient treated compared to its management with the best alternative on the market. The incremental cost includes the one for drug therapy, for other health services (for example major or minor hospitalizations due to major or minor serious side effects), for non-health services (for example support care for a patient who is not self-sufficient) and for society as a whole (for example, greater/lesser presence on the patient's work due to the disease).*
Feasibility *includes: (i) the organizational impact, i.e. the effect of a drug in managing a healthcare organizations (for example, reduction of hospital day thanks to oral replacement therapy of an injection) and (ii) the effects on adherence.*

Results

- With respect to domains priority, quality of the evidence (23%) and level of need (22%) represent the most relevant domains, followed by the type of benefit (17%) and the incremental benefit-risk profile (17%). Among panelist the view is quite homogeneous on unmet need, incremental benefit and risk and quality of evidence, even if, as expected, this last domain has a rather low relevance for patients. Instead, there is greater variability about incremental costs (greater weight attributed by payers) (Fig1).
- Focusing on absolute ranking on not comparative domains, disease severity was considered medium-high among panelist while the unmet need was perceived higher by clinicians and payers compared to patients. Thanks to good results registered in the GALLIUM trial (80% of patients with obinutuzumab survive without progression at three years[3]), the magnitude of the benefit provided by obinutuzumab was assessed as medium-high. Quality of the evidence was also judged medium-high (Tab1).
- Comparative analysis versus rituximab reports a generally neutral opinion on organizational impact (average score -0.2) and costs impact (average score 0.0) with a high variability of evaluation for this last one (positive for clinicians and patients, negative according to payers). All the panelist state a fully positive view on clinical benefit (average score +2.6) of obinutuzumab since it reduces risk of death and progression by 34%[3]. (Tab2).

Figure 1 The role of domains in the evaluation of a drug according to the panelist

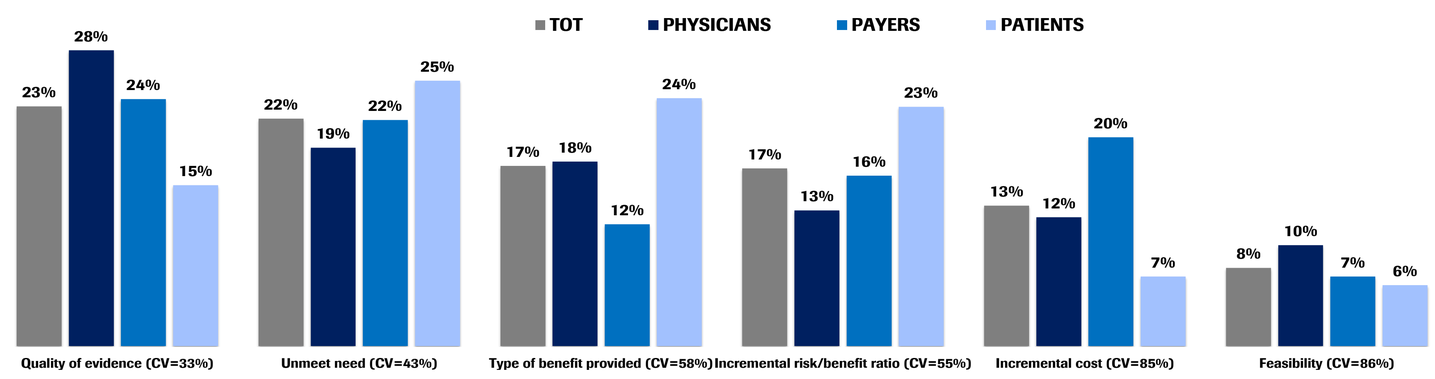

Table 1 Absolute ranking

Domains (question)		Range	Total	Physicians	Payers	Patients
Disease severity	(a)	[min 0; max 5]	3,5	3,2	3,6	3,3
Unmet need	(b)	[min 0; max 5]	2,6	2,6	3,2	1,7
Type of benefit provided	(c)	[min 0; max 5]	3,2	3,0	3,0	3,3
Quality of evidence	(d)	[min 0; max 5]	2,9	3,4	2,4	3,0

(a) It indicates the severity level of FL before obinutuzumab, between 5 (maximum severity) and 0 (minimum severity).
(b) It indicates unmet need level on FL before obinutuzumab, between 5 (maximum level) and 0 (minimum level).
(c) It indicates the magnitude of benefit provided by obinutuzumab between 5 (patient care) and 0 (no benefit).
(d) It indicates the quality of evidence of obinutuzumab between 5 (very high) and 0 (very low).

Table 2 Comparative ranking

Domains (question)		Range	Total	Physicians	Payers	Patients
Δ clinical benefit	(e)	[min -5; max +5]	2,6	2,6	2,2	2,3
Δ costs	(f)	[min -5; max +5]	0,0	1,8	-2,2	2,0
Δ organizational impact	(g)	[min -5; max +5]	-0,2	0,0	-0,6	0,3

e) It indicates the magnitude of clinical benefit of obinutuzumab compared to rituximab between +5 (maximum incremental benefit) and -5 (worsening of clinical benefit).
f) Costs differential brought by obinutuzumab compared to rituximab between +5 (substantial cost reduction) and -5 (substantial cost increase), considering only cost of drug and its management (drug cost, administration cost, follow-up cost of patients).
g) It indicates whether obinutuzumab has an organizational impact (related, for example, to the mode of administration), and quantify it between 5 (substantial improvement on organization and/or adherence compared to rituximab) and -5 (substantial deterioration on organization and/or adherence compared to rituximab).

Conclusions

- Considering patients with intermediate and high risk of progression or death (FLIPI ≥ 2) obinutuzumab reports a positive opinion on the incremental clinical benefit versus rituximab.
- Healthcare decision makers need to make trade-offs between different elements of value of new treatments. MCDA provides a framework that can be used to elicit the views of different stakeholder groups.

References

1- Evidem, Evidem Framework 10th Edition https://www.evidem.org/ (ultima data di accesso 26/2/2018).
2- Esmé G. Trevelyan J, Robinson C. Delphi methodology in health research: how to do it?", European Journal of Integrative Medicine, 7(4):423-428, 2015.
3- Marcus R, Davies A, Ando K et al. Obinutuzumab for the First-Line Treatment of Follicular Lymphoma. N Engl J Med. 2017;377(14):1331-1344.

ISPOR Copenhagen 2019