CONCEPTUAL APPROACH FOR A VALUE-BASED ASSESSMENT TOOL IN ONCOLOGY AND ITS APPLICATION IN ADVANCED TRIPLE NEGATIVE BREAST CANCER IN COLOMBIA. HTA213

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INTRODUCTION

Breast cancer (BC) **is the most common malignancy among women worldwide and remains the leading cause of cancer-related death**. In Latin America, BC is the 2nd cancer with higher mortality, is the most prevalent cancer in Colombia and from 4 women with cancer 1 of them suffer from this pathology. There are different types of technologies to treat patients with breast cancer and they vary depending on safety, efficacy, cost, impact on quality of life, etc. **One of the types of breast cancer is the advanced triple-negative breast cancer** (ATNBC) which is an aggressive type of invasive breast cancer that tends to grow and spread faster, **has fewer treatment options, and tends to have a worse prognosis**. Value frameworks in oncology are tools designed to evaluate and compare the benefits of different treatments, considering multiple criteria.

OBJECTIVE

This study aimed to develop a **value-based assessment tool** and apply it to **advanced triple-negative breast cancer (ATNBC)**, comparing Eribulin versus Capecitabine in Colombia.

METHODS

A multi-criteria matrix was developed, incorporating three attributes from ASCO's Cancer Value Framework (Advanced Disease Setting: 2020) (1) plus three additional dimensions. **The clinical attributes recognized as important by this society were supplemented with additional attributes** considered relevant by severe stakeholders in the Colombian healthcare context with different roles (non-clinical & clinical stakeholders). Similarly, the weight assigned to each attribute was determined through a consensus on their importance among these stakeholders. **The six attributes included were: Clinical Benefit, Toxicity, Bonus Points (Overall Survival tail of the curve - Treatment-Free Interval), Quality of Life (QoL), Evidence Quality and Financial Analysis**. Scores are based on the comparison of **Eribulin** and **Capecitabine** in each category: positive scores (+) favour the evaluated intervention (Eribulin), negative scores (-) favour the comparator, and zero (0) indicates equivalence.

Definitions of the Attributes Included in this Value Framework:

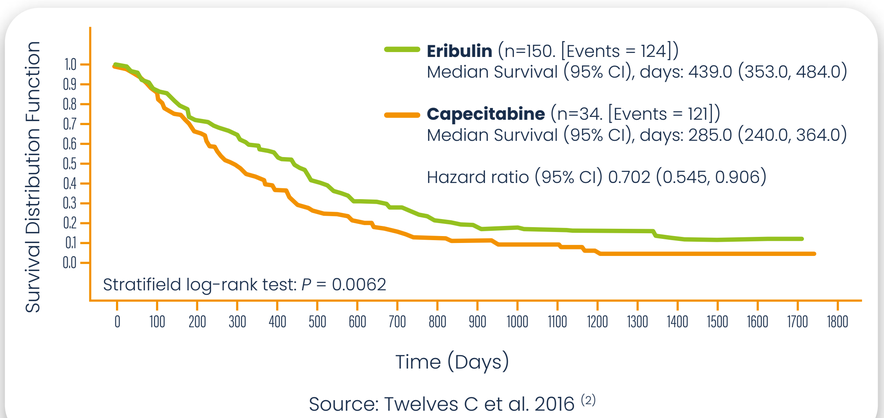
DIMENSION	DESCRIPTION	METRIC	SOURCE
Effectiveness (E)	Performance of the molecule in terms of Overall Survival regarding Hazard Ratio (HR)	(+) if HR < 1 (0) if HR = 1 (-) if HR > 1 Statistical significance p-value<0.05	Twelves et al. Basic and Clinical Research. 2016:10 77–84 doi:10.4137/BCBCR.S39615 Subgroup Analyses. (2) *
Toxicity (T)	Sum of adverse events weighted by grade and frequency according to ASCO criteria (AEi)	(+) if AEc > AEe (0) if AEc = AEe (-) if AEc < AEe c: capecitabine; e: eribulin	Kaufman, P. A et al. Journal of clinical oncology 215. 33(6), 594.(4)*
Quality of Life (QoL)	Provides a combined score between the symptom palliation bonus according to ASCO, the quality of life bonus according to ASCO and the incremental QALY	QoL= Symptoms Differential + Function Differential + QALYs Differential	Cortes et al. Breast Cancer Res Treat. 2015. 154:509–520 (3)* & authors calculations based on utility levels of PROCAN (2019) (5)
Bonus Points (BP)	Additional points awarded for Overall Survival tail (OSti) (ASCO) and treatment-free interval (ASCO).	(+) if OSte > 1.5*OStc (0) if OSte = 1.5*OStc (-) if OSte < 1.5*OStc c: capecitabine; e: eribulin	Twelves et al. Basic and Clinical Research. 2016:10 77–84 doi:10.4137/BCBCR.S39615 Subgroup Analyses.(2)*
Quality of Evidence (QoE)	Risk of Bias (RoB) based on COCHRANE Collaboration	(+) if RoBc > RoBe (0) if RoBc = RoBe (-) if RoBc < RoBe c:capecitabine; e:eribulin	Kaufman, P. A et al. Journal of clinical oncology 215. 33(6), 594. (4)*
Financial Analysis (FA)	Provides a score assessing the results of the cumulative budget impact analysis (BIA) as proportion of the annual capitation payment unit (UPC for its Spanish acronym)	(+) if BIA < -0.1% (0) if -0.1% < BIA < +0.1% (-) if BIA > 0.1%	Authors calculations based on a BIA model

***Theses studies are based on the same clinical trial: NCT00337103**

RESULTS

Eribulin was superior to Capecitabine in effectiveness, quality of life (QoL), and bonus points. Both treatments scored equally in toxicity, quality of evidence (QoE) and financial analysis. Eribulin was not inferior in any attribute.

- **Effectiveness:** No randomized clinical trial has been specifically designed to compare the primary outcome, overall survival (OS), of Eribulin versus Capecitabine in patients with advanced triple-negative breast cancer (ATNBC). Effectiveness data for this specific population were obtained from a subgroup analysis (2), where Eribulin demonstrated a significant HR (0.70),that favouring its effectiveness over Capecitabine.



Source: Twelves C et al. 2016 (2)

- **Toxicity:** This attribute was assessed using the ASCO guidelines, where both technologies received equal scores, leading to a score of zero, indicating that Eribulin and Capecitabine have both a safe profile.

		Weight	AE quantity	Score	Total Score	Difference
ERIBULIN	Frequencies of AE grade 1&2 > 10%	1	12	12	44	0
	Frequencies #AE grade 1&2 < 10%	0,5	7	3,5		
	Frequencies of AE grade 3&4 > 5%	2	3	6		
	Frequencies #AE grade 3&4 < 5%	1,5	15	22,5		
CAPECITABINE	Frequencies of AE grade 1&2 > 10%	1	10	10	44	
	Frequencies #AE grade 1&2 < 10%	0,5	9	4,5		
	Frequencies of AE grade 3&4 > 5%	2	2	4		
	Frequencies #AE grade 3&4 < 5%	1,5	17	25,5		

Based on Kaufman PA, et al. 2015 (4)

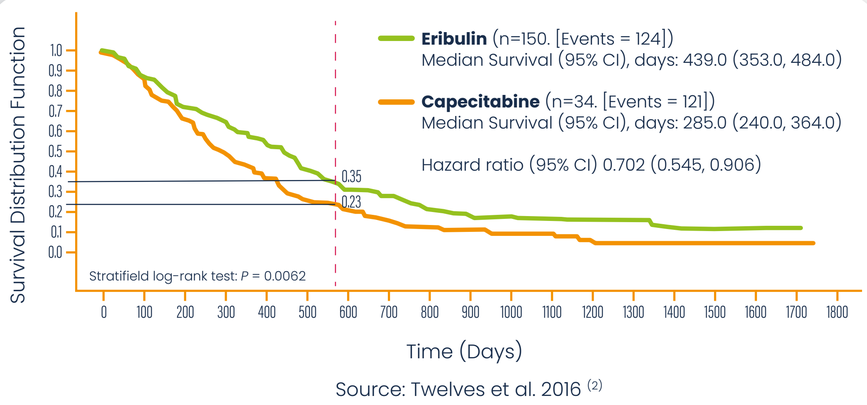
- **Quality of Life (QoL):** Among the three elements considered for this attribute, Eribulin outperformed Capecitabine in two: QoL score (Function domains) QALY increment. Number of significant symptoms was equal for Eribulin and Capecitabine.

Function Domains with significant difference (p-value < 0.05)
In favour of Eribulin (2): Future perspective & Body Image
In favour of Capecitabine (0)

Symptom Domains with significant difference (p-value < 0.05)
In favour of Eribulin (2): Diarrhea & Systemic therapy side effects
In favour of Capecitabine (2): Nausea and vomiting & Breast symptoms

Treatment	QALYs
Eribulin	0.504
Capecitabine	0.410

- **ASCO Bonus Points:** Eribulin received points for the OS tail curve; however, treatment-free interval data were not reported.



Source: Twelves et al. 2016 (2)

- **Quality of Evidence:** The quality of evidence was deemed equal for both, as they originate from the same studies (2–4). In fact, both technologies have publications across all stages, including Phase I, II, III, IV, and Real-World Evidence (RWE).
- **Financial Analysis:** The financial analysis did not show cost savings for Eribulin. However, the investment required for its use in the Colombian healthcare system for the ATNBC population would result in a minimal impact (<0.1%) on the Capitation Payment Unit (UPC). This minimal impact is considered indicative of Eribulin's non-inferiority, with a score of zero.
Budget Impact Analysis as percentage of annual capitation payment unit (UPC for its Spanish acronym)

	Year 1	Year 2	Year 3
Annual	0.0041%	0.0005%	0.0008%
Cumulative	0.04%	0.004%	0.005%

CONCLUSIONS AND DISCUSSION

*The emergence of innovative therapeutic options in oncology and their high costs lead to the need for tools that facilitate a comprehensive, multi-perspective evaluation.

*Our approach integrates classical clinical elements (efficacy and safety) with less common elements but equally important factors (quality of life, quality of evidence), alongside a financial analysis.

*The application of this new value-based assessment tool in ATNBC demonstrated that Eribulin is superior to Capecitabine in several criteria, and equal in some other within the context of the Colombian healthcare system.

*Since the comparison of overall survival was based on a subgroup analysis, due to the lack of randomized clinical trials specifically designed for the ATNBC population, conducting such trials is recommended to strengthen the findings.

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