Impact of the ESMO-MCBS v2.0 on Benefit-Risk Assessment of Emerging Therapies in Early Breast Cancer: A Comparison with the ASCO Value Framework

A. Longobardi[1], V. Molinaro[1], V. Cantile[1], R. Buonaiuto[1,2,3], A. Caltavituro[1,3], G. Crimaldi[1], M. Giuliano[1], G. Arpino[1], C. De Angelis[2]

[1]Department of Clinical Medicine and Surgery, University Federico II, Naples, Italy; [2]Scuola Superiore Meridionale - Clinical and Translational Oncology, Naples, Italy; [3]IRCCS National Cancer Institute "Fondazione G. Pascale", Department of Breast and Thoracic Oncology, Naples, Italy

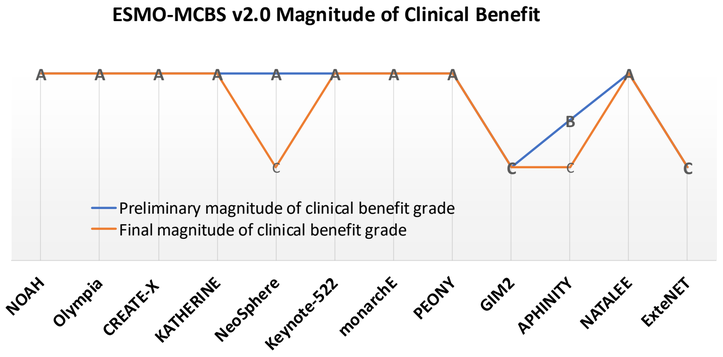
Background

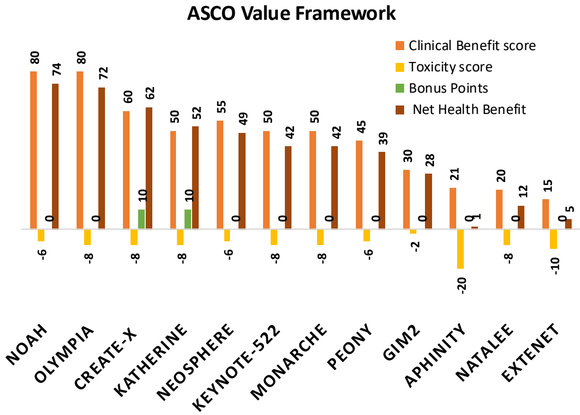
Balancing the clinical benefit and tolerability of adjuvant systemic therapies in patients with early breast cancer (eBC) remains challenging. Frameworks such as the American Society of Clinical Oncology Value Framework (ASCO VF) v2.0 and the European Society for Medical Oncology Magnitude of Clinical Benefit Scale (ESMO-MCBS v2.0) have been developed to help clinicians interpret trial results by weighing potential clinical benefit and toxicity. The European Society for Medical Oncology has recently revised ESMO-MCBS to version 2.0, which refines benefit thresholds and introduces explicit annotations for acute (AT) and persistent (PT) toxicity. This analysis applied these frameworks to evaluate the benefit-risk profiles of therapeutic strategies for high-risk eBC.

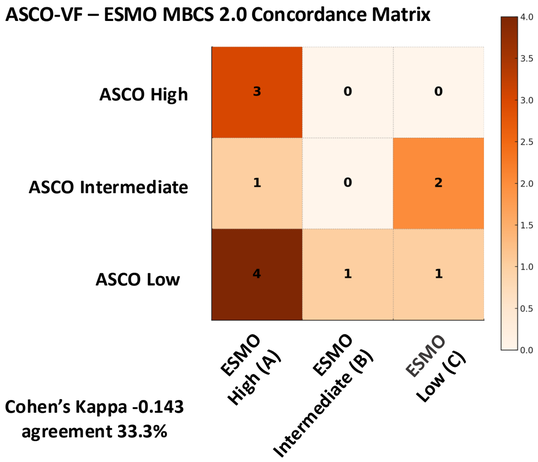
Methods and Materials

Twelve phase II-III trials (Table) were evaluated using ESMO-MCBS v2.0 and the ASCO Value Framework. Data were extracted from the latest available publications. Key endpoints included invasive disease-free survival (iDFS), overall survival (OS), pathological complete response (pCR), treatment- related adverse events (TRAEs), and quality of life (QoL). According to ESMO MBCS v2.0, standardized AT annotations for ≥30% G≥3 AEs, or ≥10% premature treatment discontinuation or hospitalization, and PT annotations for ≥20% persistent grade ≥3 toxicity, were retrieved. Concordance between ESMO MCBS and ASCO net health benefit (NHB) scores was assessed using Cohen's Kappa coefficient.

Trial	Year	Phase	Exp	Control	Primary Endpoint	Results
KATHERINE	2025	3	T-DM1	Trast	IDFS	HR 0.54 (0.44 to 0.66)
APHINITY	2025	3	Pert + Trast + CT	Placebo + Trast + CT	IDFS	HR 0.77 (0.66 to 0.91)
KEYNOTE 522	2024	3	Pembro + CT	Placebo + CT	EFS/pCR	HR 0.65 (0.51 to 0.83)
OlympiA	2024	3	Olaparib	Placebo	IDFS	HR 0.68 (0.47 to 0.97) HR+ HR 0.62 (0.49 to 0.79) HR -
CREATE-X	2024	3	Capecitabine + Standard therapy	Standard therapy	DFS	HR 0.70 (0.53 to 0.92)
ExteNET	2023	3	Neratinib	Placebo	iDFS	HR 0.66 (0.49–0.90)
monarchE	2024	3	Abemaciclib + ET	ET	IDFS	HR ITT 0.68 (0.59 to 0.77)
NATALEE	2024	3	Ribociclib + ET	ET	IDFS	HR 0.74 (0.60 to 0.91)
NeoSphere	2017	2	Trast + Doce (A)	Pert + Trast + Doce (B) Trast + Pert (C) Pert + Doce (D)	PCR	HR 0.69 (B vs A-PFS) HR 1.25 (C vs A-PFS) HR 2.05 (D vs B-PFS)
PEONY	2024	3	Pert + Trast + Doce	Trast + Doce + Placebo	PCR	HR 0.53 (EFS 3Y-EFS 5Y) HR 0.52 (DFS 3Y-DFS 5Y)
GIM2	2023	3	Dose dense CT	Non-Dose Dense CT	DFS	HR = 0.77 (0.67 to 0.89)
NOAH	2014	3	CT + Trast	CT	EFS	HR= 0.64 (0.44 - 0.63)







Results

The trials KATHERINE, NOAH, PEONY, KEYNOTE-522, CREATE-X, OlympiA, monarchE, and NATALEE achieved the highest ESMO-MCBS scores (Grade A) owing to improvements in iDFS and quality of life. In contrast, NeoSphere, APHINITY, and ExteNET were rated Grade C due to more modest absolute benefit. Notably, KATHERINE, KEYNOTE-522, OlympiA, CREATE-X, ExteNET, NATALEE, NOAH, and PEONY were annotated for acute toxicity (AT) under ESMO-MCBS v2.0, reflecting substantial rates of severe adverse events or treatment discontinuation. Among ASCO net health benefit (NHB) scores, NOAH (74), OlympiA (72), and CREATE-X (52) recorded the highest values, whereas NATALEE (12), ExteNET (5), and APHINITY (1) had the lowest scores. The APHINITY trial also showed the lowest toxicity score (-20), primarily due to the incidence of grade 3-4 diarrhea (9.8% with pertuzumab vs. 3.7% with placebo). Overall, concordance between ESMO- MCBS v2.0 and ASCO VF was limited (Cohen's Kappa -0.143; agreement 33.3%).

Conclusions

The revised ESMO-MCBS v2.0 provides a more rigorous assessment of clinical benefit by refining thresholds for absolute gains and systematically evaluating acute and persistent toxicities. NOAH and OlympiA achieved the most favorable benefit-risk balance across both tools. APHINITY and NATALEE recorded the lowest ASCO VF NHB scores, whereas APHINITY, NeoSphere and ExteNET were graded C under the ESMO-MCBS. These results emphasize differences in methodology and support the combined application of both frameworks to guide evidence-based choices in early breast cancer care.

Contact

Alessandra Longobardi, MD
Department of Clinical Medicine and Surgery, University of Naples Federico II, Naples Italy
Email: alessandra.longobardi1@gmail.com

References

1. Cherny NI, Sullivan R, Dafni U, et al. A standardized, generic, validated approach to stratify the magnitude of clinical benefit that can be anticipated from anti-cancer therapies: the European Society for Medical Oncology Magnitude of Clinical Benefit Scale (ESMO-MCBS); 2015
2. Cheng S, McDonald EJ, Cheung MC, et al. Reliability of Oncology Value Framework Outputs: Concordance Between Independent Research Groups; 2017
3. Dafni U, et al. Comparative Assessment of Clinical Benefit Using the ESMO-Magnitude of Clinical Benefit Scale Version 1.1 and the ASCO Value Framework Net Health Benefit Score; Cherny NI, de Vries EGE; 2019

This presentation is the intellectual property of the author/presenter. Contact them at alessandra.longobardi1@gmail.com for permission to reprint and/or distribute.

© Poster Template by Genigraphics® 1.800.790.4001 www.genigraphics.com