

#742; Impact of MAF selection of patients for adjuvant bisphosphonate therapy and comparison with current clinical guidance

Robert Coleman, Professor Emeritus, Department of Oncology and Metabolism, University of Sheffield, Sheffield, UK,

Roger Gomis, Cancer Science, Institute for Research in Biomedicine (IRB Barcelona), The Barcelona Institute of Science and Technology, Barcelona, Spain, (roger.gomis@irbbarcelona.org)

Alexander Paterson, Professor Emeritus, Dept of Oncology University of Calgary, Alberta Canada.

Background:

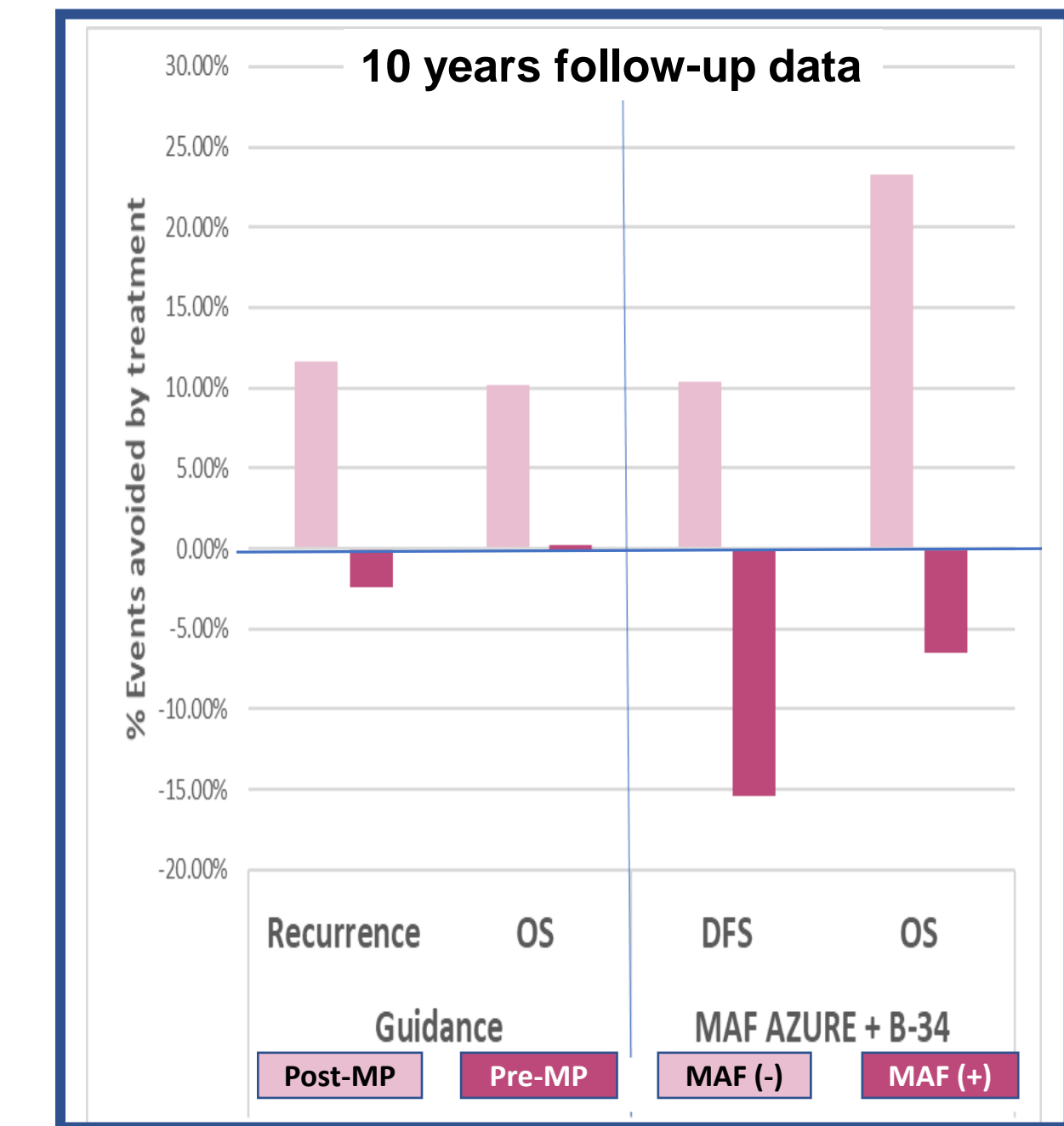
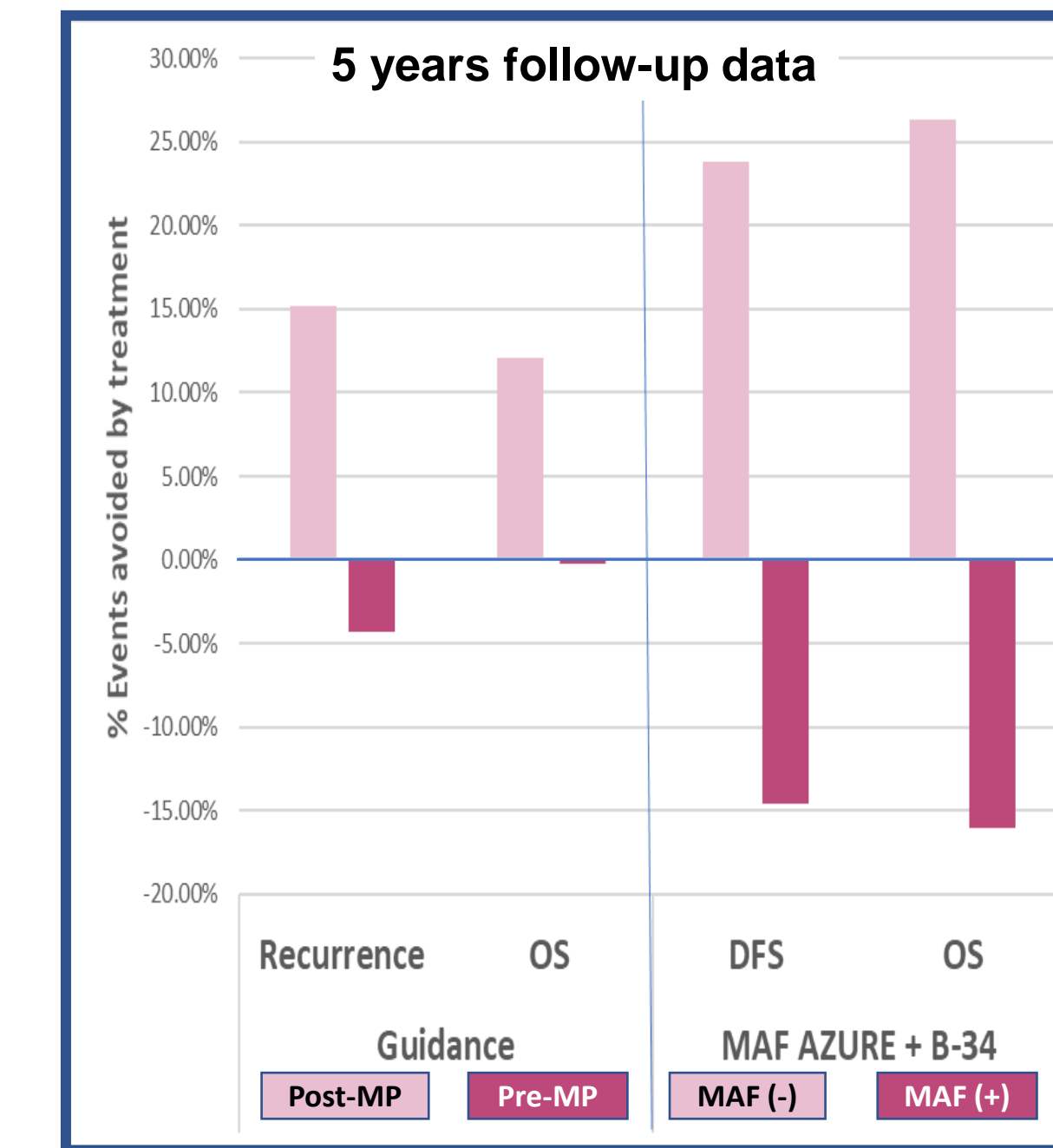
- Bisphosphonates (BP) do not have regulatory approval for use as adjuvant therapy in early breast cancer due to the failure of pivotal trials such as AZURE and NSABP B-34.
- EBCTBG¹ meta-analysis of randomized data showed clinical benefit from adjuvant BP use in postmenopausal women.
- ESMO² and ASCO³ guidelines recommend their use in this population.
- Retrospective analyses of the MAF biomarker in the AZURE⁴ (discovery) and NSABP B-34⁵ (confirmatory) trials demonstrated a significant benefit of adjuvant BP on relapse and death that was restricted to the 80% of tumors that were MAF non-amplified (MAF(-)).

5y Follow-up	Number of Patients	Patients Subgroup	Endpoint	% Pts with event Control	% Pts with event Treatment	ARR*	% events avoided by Treatment
EBCTCG** Metanalysis Stage I-III	18,766	All Pts	Recurrence	17.40%	16.30%	1.10%	6.32%
			OS	11.40%	10.60%	0.80%	7.02%
	6,171	Pre-Menop	Recurrence	20.90%	21.80%	-0.90%	-4.31%
			OS	12.90%	12.90%	0.30%	0.00%
	11,767	Post-Menop	Recurrence	15.80%	13.40%	2.40%	15.19%
			OS	10.80%	9.50%	1.20%	12.04%
AZURE + B-34 Trials Stage I-III	2,810	All Pts	DFS	18.66%	16.29%	2.37%	12.70%
			OS	9.75%	8.39%	1.36%	13.91%
	2,296	MAF -	DFS	17.05%	12.99%	4.06%	23.82%
			OS	8.88%	6.54%	2.34%	26.34%
	514	MAF +	DFS	26.52%	30.40%	-3.88%	-14.62%
			OS	13.65%	15.85%	-2.19%	-16.07%

* Absolute Risk Reduction

** Early Breast Cancer Trialists' Collaborative Group (EBCTCG) meta-analysis, Lancet 2015; 386: 1353-61

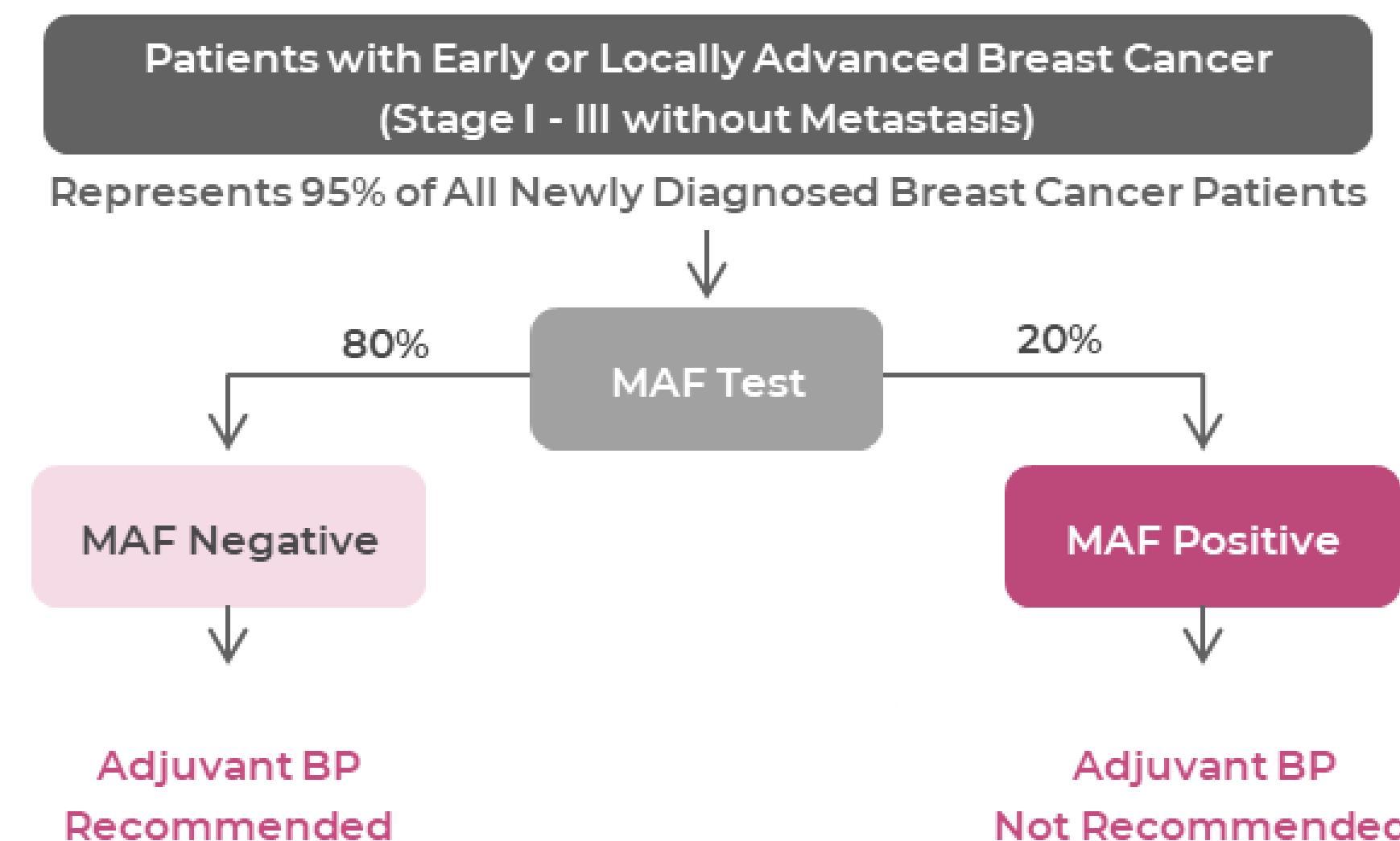
Benefits of adjuvant bisphosphonates according to stratification of early breast cancer patients by ESMO/ASCO Guidance vs MAF testing



Methods:

- We studied the relative differences in relapse and death induced by adjuvant BPs treatment in EBCTCG meta-analyses pts (stratified by pre- and post-menopausal status) compared to pts in the AZURE and B-34 trials (stratified by MAF status).
- MAF gene amplification was determined by FISH analysis on the primary tumor using the MAF Test (Inbiomotion, Spain).

Stratification based on MAF Status



Results & Conclusions:

- Clinical benefit of adjuvant BP is found only in MAF(-) patients, while for MAF(+) adjuvant BP use may be harmful.
- Stratification of early breast cancer patients according to MAF status increased the Relative Risk Reduction compared to current stratification by menopausal status recommended by current ESMO and ASCO Clinical Guidelines.
- Stratification by MAF provides a beneficial adjuvant treatment to a larger proportion of early breast cancer patients (80%) than the current indication to postmenopausal patients (63%).

References:

- Early Breast Cancer Trialists' Collaborative Group (EBCTCG). Lancet 2015; 386: 1353-61
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