ASSESSMENT OF CAPIVASERTIB FOR TREATMENT OF ADVANCED BREAST CANCER

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Background and importance

The European Medicines Agency (EMA) has recently granted approval for the use of **capivasertib**:

- Treatment of locally advanced or metastatic oestrogen receptor (ER)-positive, human epidermal growth factor receptor 2 (HER2)-negative breast cancer with PIK3CA/AKT1/PTEN alterations that hace progressed during or after endocrine therapy

Aim and objectives

To evaluate whether capivasertib and the main current standard treatments are equivalent therapeutic alternatives (ETA) by performing an indirect treatment comparison (ITC).

Material and methods

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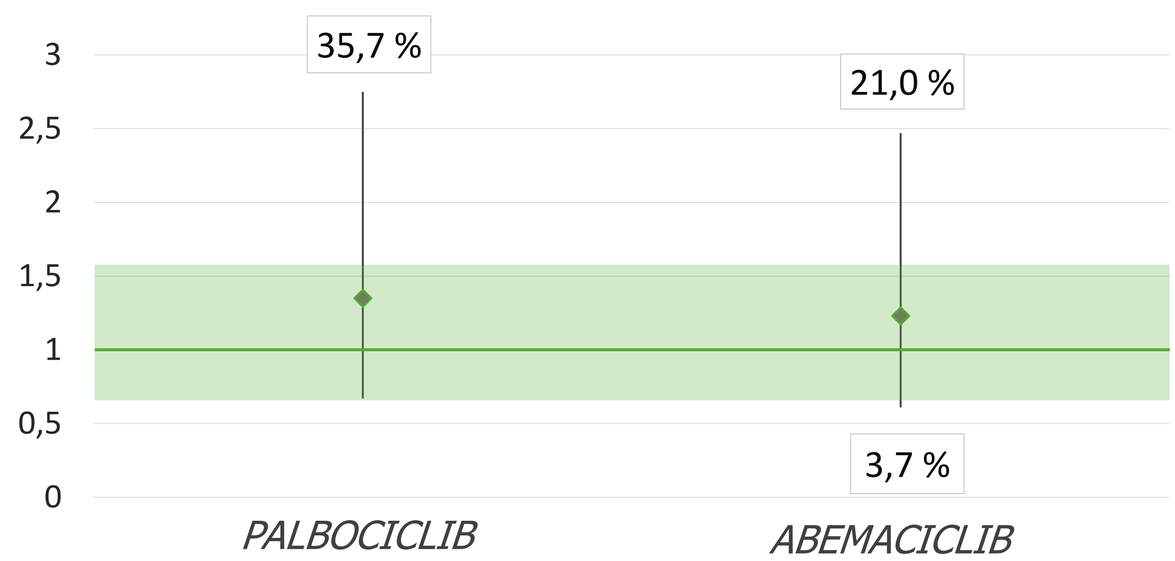
  - Treatment of **HR+ HER2-** advanced breast cancer with capivasertib, alpelisib or cyclin-dependent kinase 4/6 inhibitors in combination with fulvestrant,in patients with **PIK3CA alterations** and **progression on endocrine therapy**.
- Comparison variable: **progression-free survival (PFS).**
- **The Bucher method** was used for the ITC.
- In order to establish therapeutic the optimal therapeutic positioning, the **ETA guideline** (1) was applied.
- **Non-inferiority delta value (Δ): 0.65** (ESMO-MCBS criteria), and its inverse 1.54.
- The **Shakespeare method** was used to determine the probability of the result exceeding the equivalence Δ.

Results

- The comparison included a phase III study on **capivasertib**, one on **palbociclib**, and one on **abemaciclib**.
- Alpelisib and ribociclib were not included in the analysis as they failed to meet the established criteria for comparison.

INDIRECT TREATMENT COMPARISON (ITC) (Bucher Method)		
Progression-free survival (HR (95% CI))		
	PALBOCICLIB HR = 0,48 (95%CI 0,30 – 0,78)*	*ABEMACICLIB* HR = 0,53 (95%CI 0,33 – 0,84)*
CAPIVASERTIB HR = 0,65 (95%CI 0,38 – 1,08)*	*HR = 1,35 (0,67 – 2,75)* *p = 0,40117*	*HR = 1,23 (0,61 – 2,47)* *p = 0,56808*
**Clinical Trials results*		

Results of the clinical trials and the indirect comparison



Conclusion and relevance

- In accordance with the ETA guideline, capivasertib cannot be considered ETAs in comparison to palbociclib and abemaciclib.
- There is no evidence indicating a superior efficacy of capivasertib in combination with fulvestrant compared to palbociclib and abemaciclib in combination with fulvestrant.
- Given the toxicity profile of capivasertib, the recommended initial treatment option for of CDK4/6 inhibitors remains unchanged.

References and/or acknowledgements

(1) *Alegre Del Rey EJ et al. Med Clin (Barc) 2014 -07-22;143(2):85-90.*

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