ASSESSMENT OF REGORAFENIB, RAMUCIRUMAB AND CABOZANTINIB AS SECONDLINE THERAPY IN HEPATOCARCINOMA AND ALFA-FETOPROTEIN VALUE ≥400 NG/ML

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Background and importance

Regorafenib, ramucirumab and cabozantinib are used as a second-line therapy in patients with hepatocarcinoma and alfa-phetoprotein value ≥400ng/mL (HCC-AP≥400). There are no direct comparisons among them.

Aim and objectives

To establish whether regorafenib, ramucirumab and cabozantinib can be declared equivalent therapeutic alternatives (ATE) in the second line of HCC-AP≥400 , through an indirect treatment comparison (ITC) using a common comparator.

MATERIAL AND METHODS

A search was conducted to identify phase III clinical trials with similar populations (second line of treatment of HCC-AP≥400), duration and endpoints

If more than one study of the same drug were found, the results were combined through a meta-analysis (Joaquim Primo calculator). ITC was made according to Bucher's method

Delta value (Δ), maximum acceptable difference as a clinical criterion of no-inferiority → **0,750 (and its inverse, 1,33)** → **The value used in the trials to calculate the sample size**

The variable selected to determine clinical equivalence was overall survival (OS)

To establish the positioning, the criteria of the ATE Guide were applied. If the 95%CI deviated from the delta margin, this probability was calculated using Shakespeare method

RESULTS

Four clinical trials were found, ramucirumab (N=2), regorafenib (N=1) and cabozantinib (N=1). Ramucirumab trials were pooled, resulting in HR 0.71 (95%CI 0.58-0.86). The results of the ITC were as follows:

REFERENCE	OS: HR (95% IC)
cabozantinib-regorafenib	1.044 (0.692-1.576)
ramucirumab-regorafenib	1.044 (0.726-1.501)
ramucirumab-cabozantinib	1 (0.712-1.405)

Limitation founds: included population
(only patients with alpha-fetoprotein≥400ng/ml vs. all patients, then subgroup data were used for ITC),
and previous therapy as first line
(only sorafenib vs. other treatments allowed, in small percentages)

According to the ATE Guide, there was a likely clinical equivalence

The probability that the result exceeded the delta margin above and below was, respectively,
12.45% and 5.76% for cabozantinib-regorafenib,
9.57% and 3.71% for ramucirumab-regorafenib,
and 5% and 4.86% for ramucirumab-cabozantinib

CONCLUSION

The ITC showed no statistically differences in OS among the drugs. The 95%CI showed a certain grade of uncertainty, exceeding the equivalence margin. According to the ATE Guide, we could consider that there was clinical equivalence among the drugs due to the small percentage of the 95%CI that is outside the equivalence margin.

https://www.eahp.eu/25-2SPD-006

L01 - Cytostatics

2SPD-006