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Letter to the Editor

Experimental study on the prevention of liver cancer angiogenesis via miR-126. Promising results for targeted therapy

Dear Editor,

We read with great interest the paper written by Jing et al[1], recently published on Eur Rev Med Pharmacol Sci and titled ''*Experimental study on the prevention of liver cancer angiogenesis via miR-126* '', very interesting and promising topic based on miR-126 therapy.

Furthermore, recent issues reporting the exact identification of cellular signaling pathways playing a key role in the angiogenesis have led to development of new molecules for targeted therapies[2]. This research is very important and could open future scenarios for the planning of targeted therapies coupling miR-126 and novel angiogenesis inhibitors[3].

To date, due to novel drugs (Table I) and more pathological knowledge in the outcome of hepatocellular carcinoma (HCC), patients have improved also in so called "frail patients"[4]. Unfortunately, insufficient data are reported also in clinical trials in HCC patients who carrying concomitant HIV/HCV/HBV infections and liver metabolic disease[5-8] .

Considering the heterogeneous aspects of HCC and to enhance therapeutic efficacy, overcome drug resistance and reduce toxicity, combination of antiangiogenic drugs with antiblastic chemotherapy (AC), radiotherapy or other targeted drugs as miRNAs, have been evaluated[9]. To date, there is no designed approach to determine which patients are most likely responsive to a given type of antiangiogenic treatment based on miRNAs molecules.

However, another aspect will be focusing on the miRNAs and in particular miR-126 is the efficacy of their detection[10]. Moreover, if the detection of miR-126 is routinely incorporating into clinical practice, knowledge concerning the predictive value of this test will eventually enable individual therapy in HCC patients[11].

Several approaches to consider the quality of the treatments for suitable cost-effective models into healthcare systems are ongoing consideration in HCC managements[12].

Finally, the results obtained by Jing et al[1] are interesting, but, in our opinion, need of more confirmation studies, considering the high incidence of HCC and its tissue heterogeneity in human model.

In addition, we think that the recent progress in genetics have provided exceptional opportunities to identify prognostic and predictive markers of efficacy of antiangiogenic treatments[13]. Genetic markers could be a tool to identify patients who will benefit from this targeted therapy, and exclude patients with high risk to develop severe toxicity[14].

We know that this kind of translational studies are strongly recommended to have more and more information on HCC with the aim to improve the efficacy of treatment and quality of patients life[15]. This field of research might be able to accelerate the translational research into the routine therapies.

Conflict of interest

The Authors declare that they have no conflict of interests.

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Table I. Most common antiangiogenic molecules used in HCC.

Drugs (Alias)	Typology	Targets	HCC therapeutic indication and study phase
Bevacizumab	Monoclonal antibody	VEGF	Phase II study in combination with Erlotinib (NCT00881751)
Brivanib	Small molecule Multikinase inhibitor	VEGFR, FGF	Advanced stage, Phase III study in patients who failed Sorafenib (NCT00825955), and first line (NCT00858871)
Cabozatinib	Small molecule Multikinase inhibitor	c-MET, RET, VEGFR1-3, c-KIT,	Preclinical study, yet.
Cediranib	Small molecule Multikinase inhibitor	VEGFR 2, PDGFR, c-Kit	Advanced stage, phase II study
Everolimus	Small molecule	m-TOR	Not registered; phase III study did not show significant efficacy
Lenvatinib	Small molecule Multikinase inhibitor	VEGFRs 1, 2 and 3, FGFRs 1 PDGFRα, RET, KIT	Not registered; phase III trial underway (NCT01761266)
Linfantib	Small molecule Multikinase inhibitor	VEGFR 2, PDGFR families	Advanced stage, phase III study first-line vs sorafenib (NCT01009593)
Nintedanib	Small molecule Multikinase inhibitor	VEGFRs 1, 2 and 3, FGFRs 1 PDGFR	Phase design study vs sorafenib (NCT00987935 and NCT01004003)
Ramucirumab	Monoclonal antibody	Selective VEGFR 2	Not registered; phase III study with conflicting results
Refametinib	Small molecule Mitogen-activated protein kinase inhibitor	MEK 1-2	Advanced stage, phase II study in patients who failed sorafenib (NCT01915589) and in combination with sorafenib (NCT01915602)
Regorafenib	Small molecule Multikinase inhibitor	VEGFR1-3, c-KIT, TKIg-like, EGF-like 2, PDGF 2, FGF 1, RET, RAF-1, BRAF, MAPK	Not registered; phase III study underway recruiting patients who progressed under sorafenib (NCT01774344).
Sorafenib	Small molecule Multikinase inhibitor	VEGFR 2, PDGFR, c-Kit, BRAF	Advanced stage; not recommended for use in adjuvant treatment
Trebananib	Small molecule Angiogenesis inhibitor	Tie-2 (Angiopoietin)	Not registered; phase II study no showed improvement of OS.
Vatalanib	Small molecule Angiogenesis inhibitor	VEGFRs 1, 2 and 3, PDGFR c-FMS	Advanced stage, phase II in combination with Doxorubicin.

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