

# Cavity development: a potential biomarker for antiangiogenesis agents

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Cecere FL, Aguilar A, Rosell R. Lung cavitation in lung metastases of gastric and non-small-cell lung cancer patients treated with apatinib. Transl Lung Cancer Res 2019;8:317-8.

McKay MJ. What's in a (tumor) cavity? Transl Lung Cancer Res 2020;9:8-9.

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Thanks for the editors. Thanks for all the suggestions (1,2). The fish models should be modified to further explain the mechanism. The studies about the influence of cavity development on inflammatory, metastatic and autophagy were going on.

As we all known, lung cavity is the commonest phenomena in patients treated with antiangiogenesis agents (3-6). As our observation, pulmonary lesions generated cavity may be due to "spill-over abscess" and "cavity necrosis" (7).

An important reason to cavity information was "spillover abscess". According to baseline data, all patients were in III or IV stage, and all patients with vascular involvement were response for lung cavity generated. As we all known, vascular involvement usually led to gradual bronchial obstruction which will end as tumor necrosis.

Another reason for cavity generated, especially to patients without vascular involvement was cell necrosis. The cell experiments showed that apatinib lead to tumor cells breakdown of the growth, making the proliferation inhibition (6). It has been indicated that antiangiogenesis agents usually lead to generate a lot of apoptotic cells. The antiangiogenic property will cause lacking of support to cell growth, which aggravated the tumor cells necrosis. These mechanisms, both vessel growth inhibition and proliferation inhibition combined inducing the lung cavity information. Furthermore, as the cell experiments showed, under hypoxic conditions, apatinib could not inhibit the protein expression of VEGFR and HIF- $\alpha$ , indicating the cell necrosis will be limited when lung cavity generated.

In our follow-up study, after stop antiangiogenic therapy, subsequent fill-in phenomenon can be observed in many patients who did not receiving any adjuvant radiotherapy. And all patients with radiation pneumonitis did not return to normal. This means the infection in lung will influence the recovery of lung.

In conclusion, lung cavity may mean effective disease control in pulmonary lesions, and it is a reversible process in antiangiopathy. While in apatinib therapy, infection prevention will be paid special attention to ensure patients taking continuous benefits.

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# Footnote

*Conflicts of Interest:* The authors have no conflicts of interest to declare.

*Ethical Statement:* The authors are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

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