[\textsuperscript{153}Sm]Samarium-labeled FAPI-46 radioligand therapy in a patient with lung metastases of a sarcoma

Clemens Kratochwil\textsuperscript{1} · Frederik L. Giesel\textsuperscript{1} · Hendrik Rathke\textsuperscript{1} · Rebecca Fink\textsuperscript{1} · Katharina Dendl\textsuperscript{1} · Jürgen Debus\textsuperscript{2} · Walter Mier\textsuperscript{1} · Dirk Jäger\textsuperscript{3} · Thomas Lindner\textsuperscript{1} · Uwe Haberkorn\textsuperscript{1,4,5}

Image of the month

Fibroblast activation protein is overexpressed by cancer-associated fibroblasts (CAFs) in the stroma of several tumor entities and provides anti-immunogenic effects [1]. It can be targeted with radiolabeled small-molecule inhibitors (FAPIs) [2].

This image demonstrates a patient with progression of lung metastatic, fibrous spindle cell soft tissue sarcoma. Primary tumor located between bladder and rectum as well as early generations of oligo-focal metastases had previously been treated by resection and external-beam radiotherapy. In systemic stage, mutanom-based vaccination [3], cyclophosphamide, and pazopanib had already been used but the patient was considered inappropriate for standard chemotherapy with anthracyclines. An interdisciplinary tumor conference considered experimental FAPI-RLT a promising option for this therapy-refractory patient to serve as a “can opener” for succeeding immunotherapy.

FAPI-PET/CT demonstrated target positive tumor phenotype (a). Due to the relatively short biological tumor half-life of quinoline-based FAPI-46 [1], it was labeled with short physical half-life (46.3 h) \textsuperscript{153}Sm. Emission scans during therapy demonstrate tumor targeting up to 44 h p.i. and rapid clearance from normal organs (b). Three cycles with cumulative 20 GBq \textsuperscript{153}Sm- and 8 GBq Y-90-FAPI-46 (\textsuperscript{153}Sm was not available with sufficiently high specific activity) were well tolerated and achieved stable disease for 8 months (c). Next treatment lines were pembrolizumab, experimentally enhanced with oncolytic parvovirus [4], and nab-paclitaxel. Under both therapies, the patient progressed after only 3 months.

One explanation for the clinical activity of \textsuperscript{90}Y/\textsuperscript{153}Sm-FAPI-46 in this particular case might be FAP expression in both CAFs and sarcoma tumor cells [5], which is unfortunately not the case in other tumor entities. Of course, one case is no proof of general efficacy but obviously this image encourages further studies of FAPI-RLT against soft tissue sarcoma. However, due to technical issues related to \textsuperscript{153}Sm, e.g., regarding specific activity and contamination with \textsuperscript{154}Eu, additional short physical half-life isotopes should be evaluated as alternative options.
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Declarations

Conflict of interest  TL, UH, CK, and FLG have a patent application for FAPI-ligands. TL, UH, CK, and FLG also hold shares of a consultancy for iTheranostics.

Ethics approval  This image presents a case report from clinical practice and does not require IRB approval or registration as a clinical trial.

Consent to participate/consent for publication  Patient gave written informed consent to receive experimental therapy and anonymized publication of this case.

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References

1. Liu R, Li H, Liu L, Yu J, Ren X. Fibroblast activation protein: a potential therapeutic target in cancer. Cancer Biol Ther. 2012;13(3):123–9. https://doi.org/10.4161/cbt.13.3.18696.
2. Giesel FL, Kratochwil C, Lindner T, et al. 68Ga-FAPI PET/CT: biodistribution and preliminary dosimetry estimate of 2 DOTA-containing FAP-targeting agents in patients with various cancers. J Nucl Med. 2019;60(3):386–92. https://doi.org/10.2967/jnumed.118.215913.
3. Türeci Ö, Vormehr M, Diken M, Kreiter S, Huber C, Sahin U. Targeting the heterogeneity of cancer with individualized neoepitope vaccines. Clin Cancer Res. 2016;22(8):1885–96. https://doi.org/10.1158/1078-0432.CCR-15-1509.

4. Ungerechts G, Engeland C, Buchholz CJ, et al. Virotherapy research in Germany: from engineering to translation. Hum Gene Ther. 2017;28(10):800–19. https://doi.org/10.1089/hum.2017.138.

5. Dohi O, Ohtani H, Hatori M, Sato E, Hosaka M, Nagura H, et al. Histogenesis-specific expression of fibroblast activation protein and dipeptidylpeptidase-IV in human bone and soft tissue tumours. Histopathology. 2009;55(4):432–40. https://doi.org/10.1111/j.1365-2559.2009.03399.x.

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