



RESEARCH TOPIC-MEM11
CANCER-ASSOCIATED FIBROBLASTS ROLE AND PET/CT IMAGING IN REFRACTORY AND RELAPSED HODGKIN DISEASE

Curriculum MEM Clinical

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Abstract

Cancer-associated fibroblasts (CAFs) trigger several pro-tumorigenic signalling pathways. Fibroblast activation protein α is overexpressed on CAF surface and tumour stroma and has been identified as a feasible target for therapy and molecular imaging using FAP-specific PET/CT.

CAF play a crucial role in the onset of resistance to chemotherapy in refractory/relapsed Hodgkin lymphoma.

The aim of the project is the identification of cancer-associated fibroblast biomarkers in prediction of refractory/relapsed Hodgkin lymphoma.

Hodgkin lymphoma patients' candidates to first-line chemotherapy will be enrolled to correlate fibroblasts tissue biomarkers with FAPI-specific imaging. Patients will undergo FAPI PET/CT evaluation at baseline and end-of-treatment. Lymph node tissue samples will be analysed to identify cancer-associated fibroblasts specific biomarkers on fibroblast surface and in the extracellular matrix. FAPI PET/CT semi-quantitative data and molecular biology data will be matched with clinical, serum marker, FDG PET/CT semi-quantitative data and follow-up.

Main technical approaches

Pathological analyses of lymph-nodes, analyses of circulating biomarkers, synthesis of [68Ga-]Ga-DOTA-FAPI, imaging analysis of FAP PET/CT

Scientific references

1. Moskowitz AJ, Perales M-A, Kewalramani T, Yahalom J, Castro-Malaspina H, Zhang Z, et al. Outcomes for patients who fail high dose chemoradiotherapy and autologous stem cell



rescue for relapsed and primary refractory Hodgkin lymphoma. *Br J Haematol.* 2009 Jul;146(2):158–163.

2. Aldinucci D, Celegato M, Casagrande N. Microenvironmental interactions in classical Hodgkin lymphoma and their role in promoting tumor growth, immune escape and drug resistance. *Cancer Lett.* 2016 Sep 28;380(1):243–252.

3. Raffaghello L, Vacca A, Pistoia V, Ribatti D. Cancer associated fibroblasts in hematological malignancies. *Oncotarget.* 2015 Feb 20;6(5):2589–2603.

4. Nurmik M, Ullmann P, Rodriguez F, Haan S, Letellier E. In search of definitions: Cancer-associated fibroblasts and their markers. *Int J Cancer.* 2020 Feb 15;146(4):895–905.

5. Kratochwil C, Flechsig P, Lindner T, Abderrahim L, Altmann A, Mier W, et al. 68Ga-FAPI PET/CT: Tracer Uptake in 28 Different Kinds of Cancer. *J Nucl Med.* 2019 Apr 6;60(6):801–805.

Type of contract

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