BACKGROUND
Fusion between FGFR3 and TACC3 represents a rare acquired resistance mechanism following treatment with EGFR TKIs. Data regarding its prevalence and therapeutic implication is limited (Ref. 1-3).

OBJECTIVES
• FGFR1/2/3 fusion prevalence in aNSCLC de novo and
• FGFR1/2/3 fusion prevalence in aNSCLC as a resistant mechanism following EGFR TKIs in EGFR mutant (EGFR M) aNSCLC.
• Activity of the EGFR TKI+FGFR TKI combination following progression of EGFR TKIs in EGFR M aNSCLC.

RESULTS
• In GH ED, the prevalence of FGFR2 and FGFR3 fusions were 0.02% and 0.26%, respectively.
• Of FGFR3 fusions, 99.3% were FGFR3-TACC3 (Figure 1).
• Of FGFR3-TACC3 fusions, EGFR mutations co-existed in 23% (exon 19 del, 66%; L858R, 31%; L851Q, 3%) (Figure 2).
• In TASMC, 1 case of de novo FGFR3-TACC3 fusion was detected (prevalence, 0.2%).
• Of 3 patients with FGFR3-TACC3 fusions following progression on EGFR TKIs (2 females, age 59-84y; EGFR mutation type: E746_A750del, L858R, L747_A750delinsP) (Table 1), 2 patients received gefitinib/erdafitinib and osimertinib/erdafitinib combinations with a disease stabilization and a partial response for 4 and 2+ months, respectively (Figure 3).

Figure 1. FGFR2/3 fusion subtypes distribution in aNSCLC.

Figure 2. Prevalence of co-existing EGFR activating mutations in the patients with aNSCLC and FGFR1-TACC3 fusions.

Figure 3. FDG-PET/CT images before (A) and during (B) therapy with osimertinib/erdafitinib in a patient with an EGFR M aNSCLC and FGFR3-TACC3 fusion progressing on osimertinib. Shrinkage of a retro-caval lymph node with a reduction in FDG-avidity, stable lung metastasis with a reduction in FDG-avidity, sclerostesis of a D3 lytic metastasis with a reduction in FDG-avidity.

Table 1. Demographic and clinico-pathological characteristics of patients with EGFR M aNSCLC progressing on EGFR TKIs and developing an FGFR3-TACC3 fusion.

METHODS
• Retrospective analysis.
• Ofard Health (GH) de-identified electronic database (ED) (11/2016-07/2021) - prevalence of FGFR2/3 fusions with and without co-existing EGFR mutations (assuming co-existing mutations reflect the status of acquired FGFR fusion-driven resistance to EGFR TKIs in EGFR M aNSCLC);
• aNSCLC ED of TASMC (06/2020-06/2021) - prevalence of de novo FGFR1/2/3 fusions.
• Case-series of patients with EGFR M aNSCLC progressing on EGFR TKIs and developing an FGFR3-TACC3 fusion selected from Davidoff Cancer Center (DCC) and Oncology Department, Bnei-Zion hospital (BZ) ED (04/2014-04/2021, n=3) - clinico-pathological characteristics, systemic therapies and outcomes.

CONCLUSIONS
• FGFR3-TACC3 fusions are the most common FGFR fusion subtype in aNSCLC.
• Up to 23% of FGFR3-TACC3 fusions in aNSCLC are associated with a co-existing EGFR M, possibly representing an acquired resistance following treatment with EGFR TKIs.
• In this clinical scenario, combination of existing EGFR TKIs and FGFR TKIs represents a promising treatment strategy.

References