PROGNOSTIC VALUES OF DIFFERENT SUBTYPES OF KRAS MUTATIONS IN PANCREATIC CANCER
Authors: S. Smirnov, H. Subach, K. Hukhouskaya, K. Grenza, A. Portyanko.
N. N. Alexandrov National Cancer Centre of Belarus

BACKGROUND
Mutated KRAS is considered as a negative prognostic marker for survival in pancreatic ductal adenocarcinoma (PDAC). However, prognostic values of individual mutations (G12D, G12V or G12R) are still controversial. The aim of current study is to evaluate the survival of pancreatic cancer patients with different subtypes of KRAS mutations.

MATERIAL AND METHODS
Tumor tissue was obtained from 109 patients (pts) with PDAC stage I-IV (stage I – 6 pts, stage II – 27 pts, stage III – 19 pts, stage IV – 57 pts) treated at the N.N. Alexandrov National Cancer Centre of Belarus in 2019. Median follow up period was 6 month. To investigate KRAS mutations (G12D, G12V, G12R) polymerase chain reaction with TaqMan probes was performed. Statistics: exact Fisher’s test, Log-rank test.

RESULTS
- KRAS mutations were detected in 69% of samples. The distribution of different subtypes of KRAS mutations was: G12D 47%, G12V 40%, G12R 13%.
- There were no significant differences in sex, age, stage distribution, and surgical resection rate depending on KRAS status.
- KRAS-mut PDAC more frequently located in the head of the pancreas (46.7% vs 26.5%, p=0.06) than WT (figure 1).
- G12V PDAC had lymph node involvement more frequently than WT (96.2% vs 66.7%, p=0.01) or G12R (96.2% vs 55.6%, p=0.01) (figure 2).
- In stage IV PDAC bone metastasis at diagnosis more often detected in WT pts than in KRAS-mut (16.6% vs 2.6%); lung metastasis were not detected at diagnosis in pts with G12V metastatic PDAC (table 1).

CONCLUSION
There was no statistical difference in overall survival (OS) between any of KRAS groups and WT in stages I-II and III-IV PDAC.
Medium OS was significantly different between G12R and G12D unresectable PDAC stages III-IV (322 days vs 384 days, p=0.05).
One-year survival rate for pts with PDAC stages III-IV was better in WT group than G12D (33% vs 5%; p<0.05).
Chemotherapy was significantly associated with better OS in pts with unresectable PDAC stages III-IV in WT, KRAS-mut and G12D groups (p<0.01) but not in G12V (p=0.5) (figure 3).

Figure 1 – Distribution of different genetic subtypes PDAC according to ICD-10 diagnosis code (C25.0, C25.1, C25.2).

Figure 2 – Lymph node involvement in different KRAS subtype PDAC.

Table 1 – Metastasis localization at diagnosis in patients with stage IV PDAC.

![Cumulative Proportion Surviving (Kaplan-Meier)](image)

Research supported by BFFI grant NM202M-114
Contact e-mail: Genelab.omr@gmail.com