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PROGNOSTIC VALUES OF DIFFERENT SUBTYPES OF KRAS MUTATIONS IN PANCREATIC CANCER

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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%;). Also lung metastasis were not detected at diagnosis in pts with G12V metastatic PDAC (table 1).

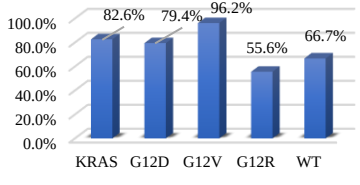

Figure 2 – Lymph node involvement in different *KRAS* subtype PDAC.

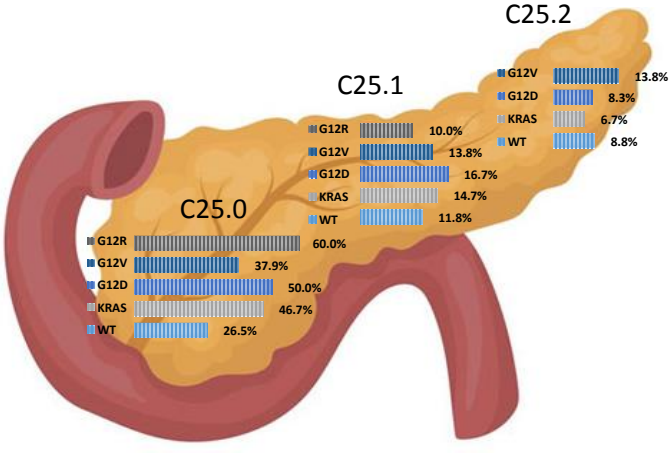

Figure 1 – Distribution of different genetic subtypes PDAC according to ICD-10 diagnosis code (C25.0, C25.1, C25.2).

Mts localization / Genetic subtype	Liver	Bone	Distant lymph node	Lung	Peritoneal
WT	83,3% (20/24)	16,6% (4/24)	16,6% (4/24)	12,5% (3/24)	8,3% (2/24)
KRAS-mut	81,6% (31/38)	2,6% (1/38)	10,5% (4/38)	15,8% (6/38)	15,8% (6/38)
G12D	77,7% (14/18)	5,5% (1/18)	11,1% (2/18)	22,2% (4/18)	16,7% (3/18)
G12V	80% (12/15)	-	13,3% (2/15)	-	20% (3/15)
G12R	100% (5/5)	-	-	40% (2/5)	-

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

- There was no statistical difference in overall survival (OS) between any of KRAS groups and WT in stages I-II and III-IV PDAC.
- Median OS was significantly different between G12R and G12D unresectable PDAC stages III-IV (322 days vs 104 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).

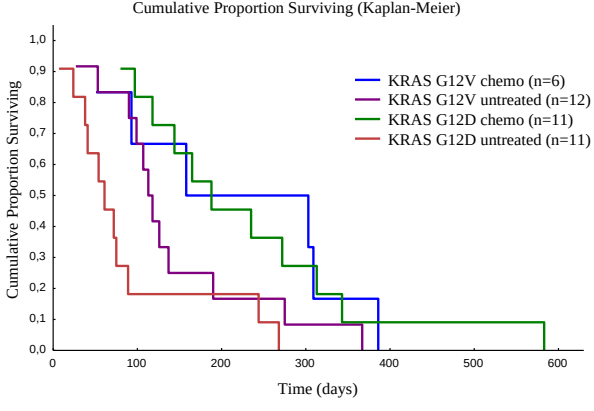

Figure 3 – Overall survival of unresectable PDAC patients stages III-IV with KRAS G12D and G12V mutations in chemotreated and chemonaive groups.

CONCLUSION

We found no significant association between mutated KRAS and OS in PDAC pts, possible due a small sample size. However, pts with G12D mutation had worse one-year survival rate and lower OS than pts with other subtypes of KRAS mutation.

Research supported by BFFI grant №M20M-114

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