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SPOP and *FOXA1* alterations in prostate cancer. Relationship with *ERG* overexpression and grade group classification

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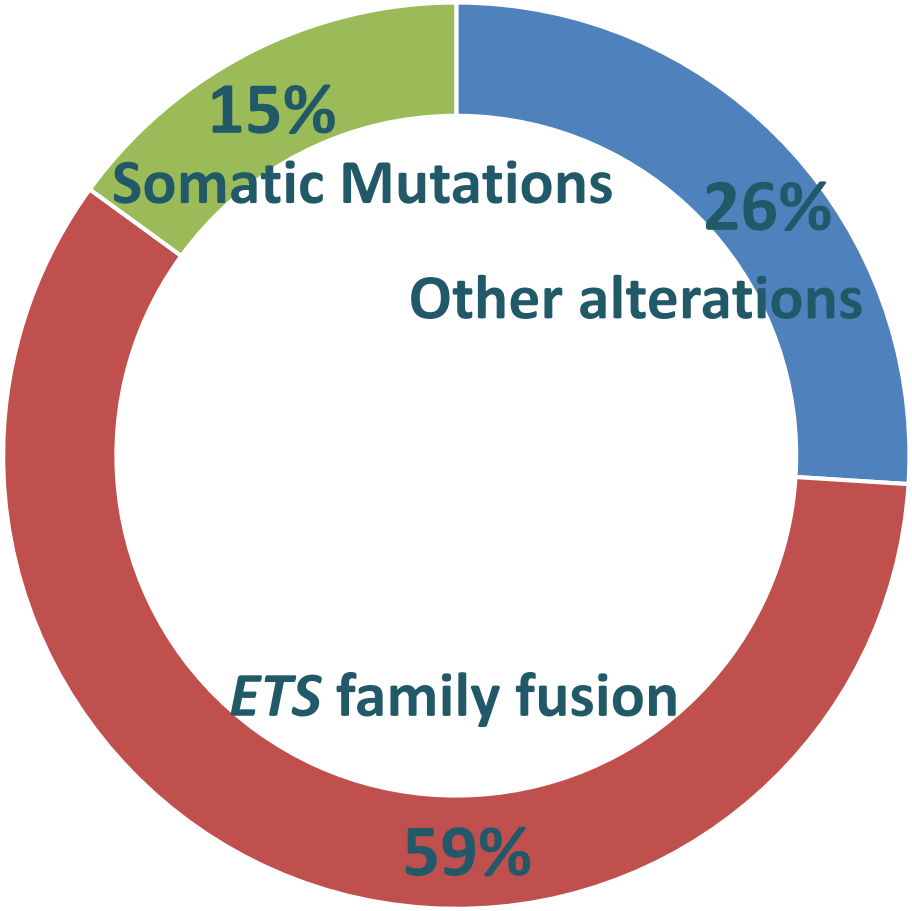
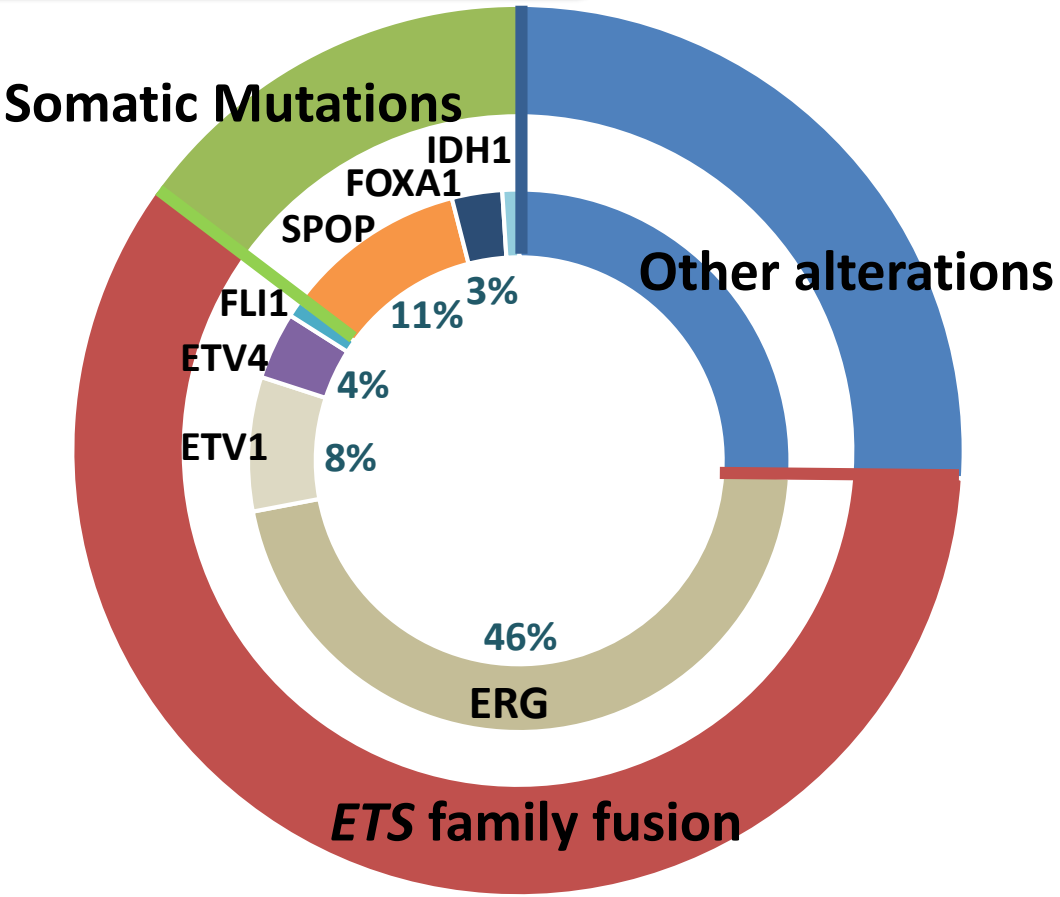
Prostate cancer: Two pathways

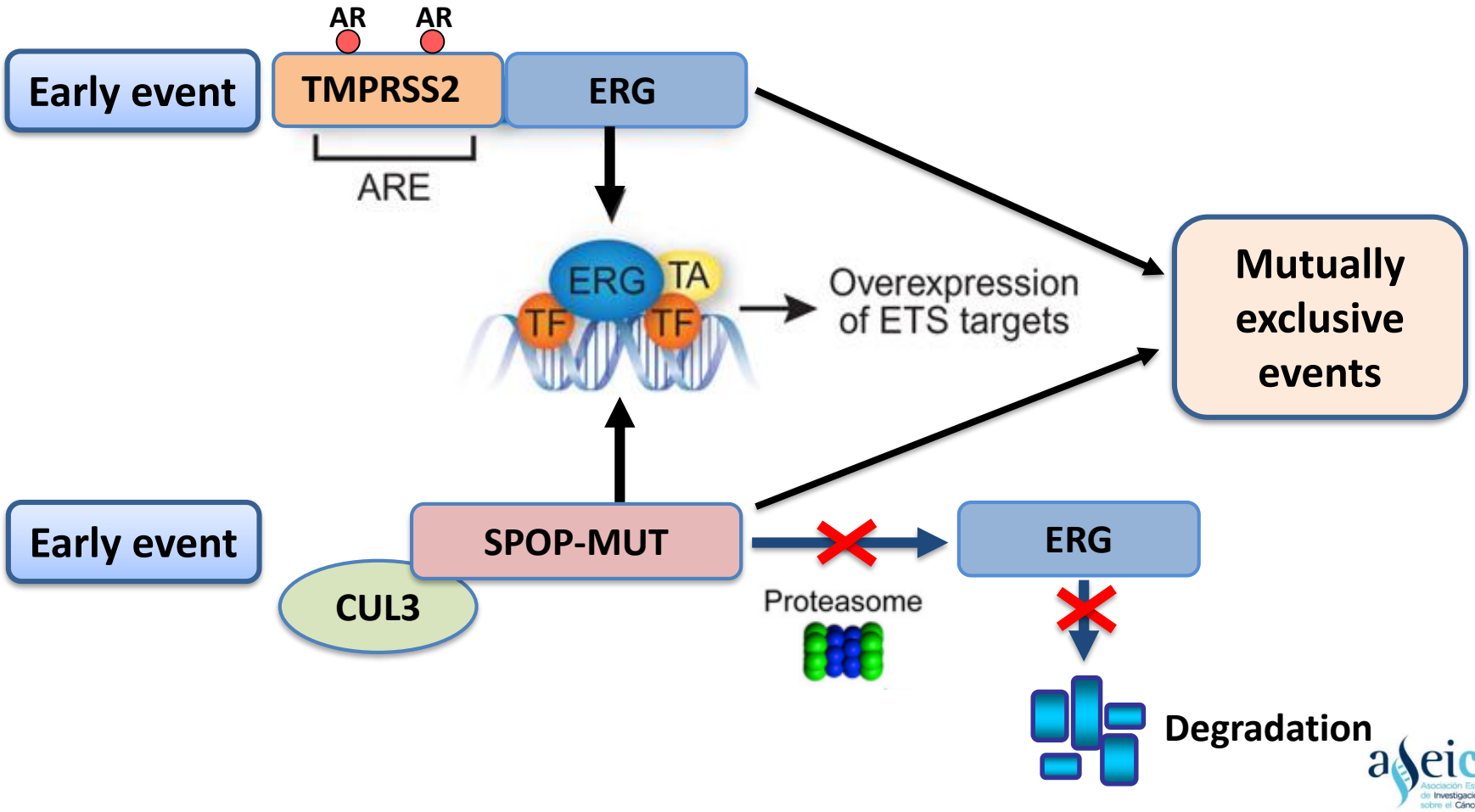


The Cancer Genome Atlas (TCGA) 2015



The Cancer Genome Atlas Research Network, Cell 2015

Prostate cancer: *ERG* rearrangements or *SPOP* mutations



Objectives

To analyze the prevalence of *SPOP*, *FOXA1* and *IDH1* alterations in PrCa, and to determine the relationship of these alterations with *ERG* status, and with the different clinical and pathological variables.

Material and Methods

Tumor samples and patients

Parc de Salut MAR-MarBiobank

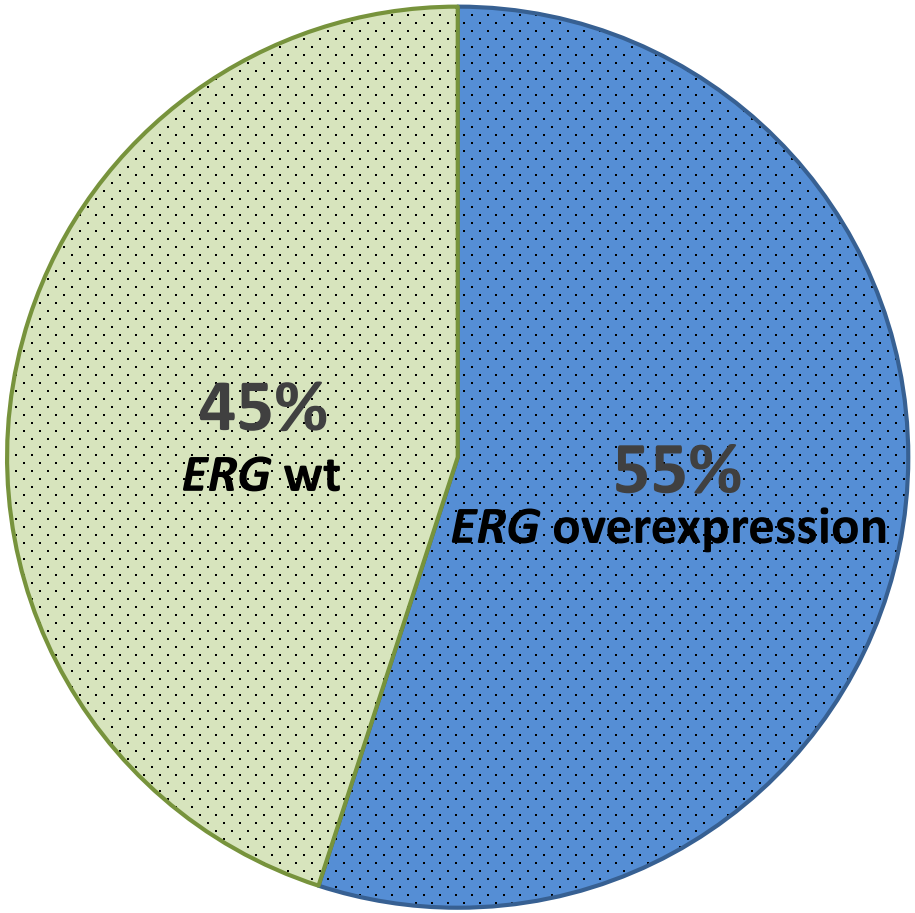
Frozen prostate tumors = 111
non-tumor prostate samples = 3

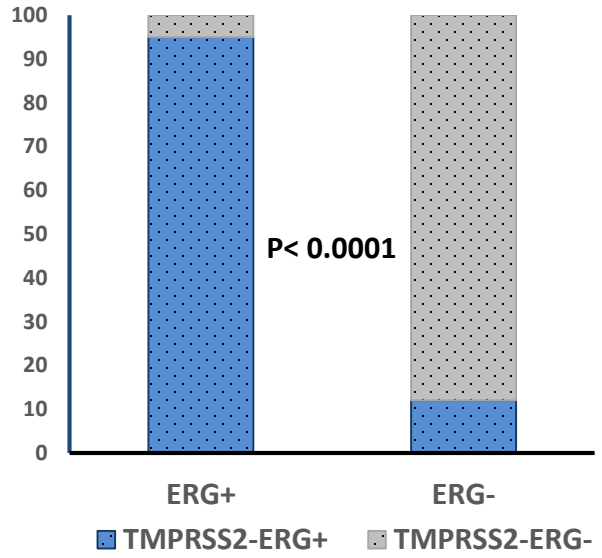
WHO-ISUP (2016)
GG1= 28
GG2= 34
GG3= 21
GG4= 17
GG5= 11

Methods

- RNA extraction and RT
- *TMPRSS2-ERG*, *ERG*, *SPOP* qPCR (TaqMan® Gene Expression Assays)
- *GADPH* as internal control
- *SPOP, FOXA1* and *IDH1* mutational analysis
- Kaplan-Meier test

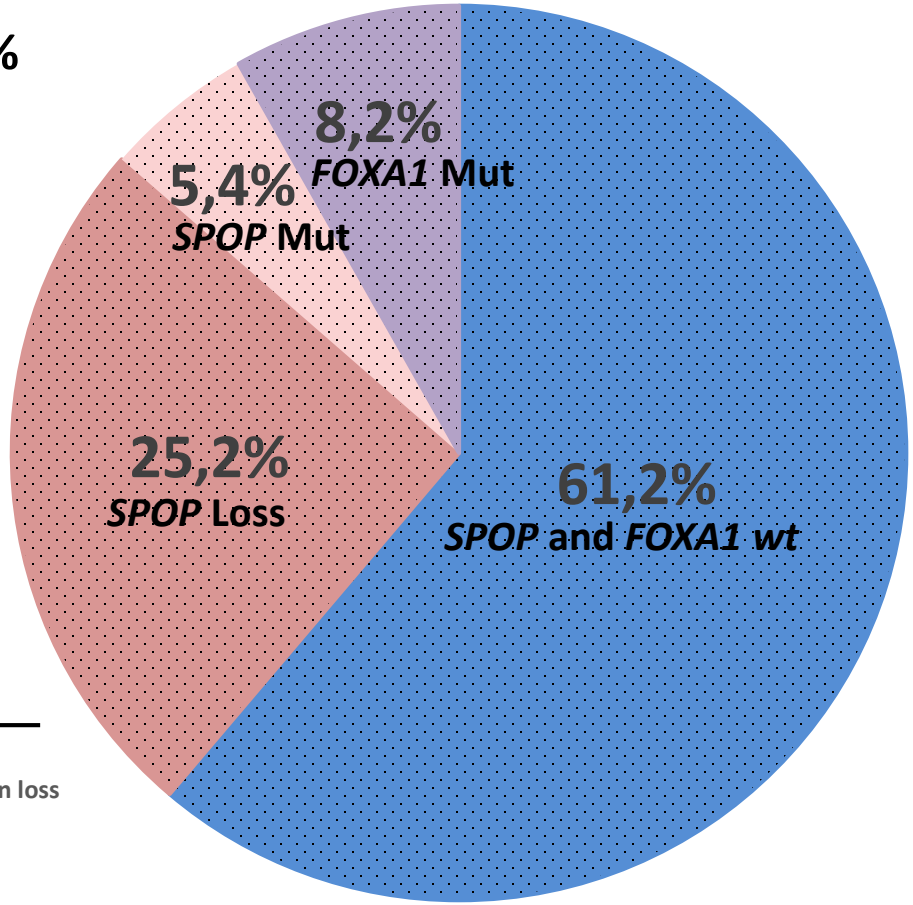
TMPRSS2-ERG and *ERG* overexpression in prostate cancer

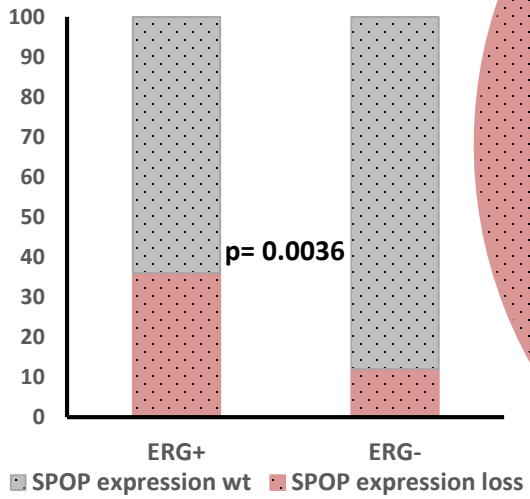


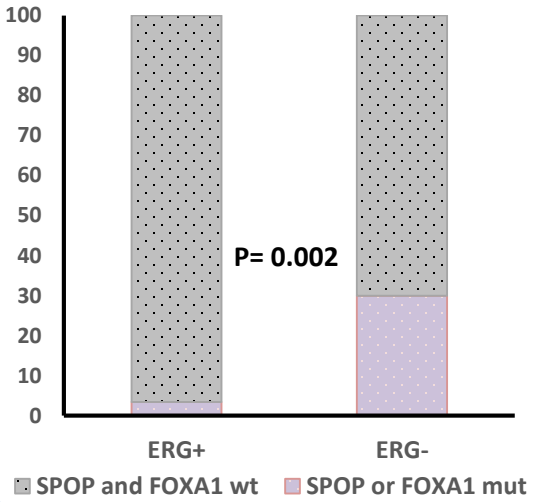


SPOP and *FOXA1* alterations in prostate cancer

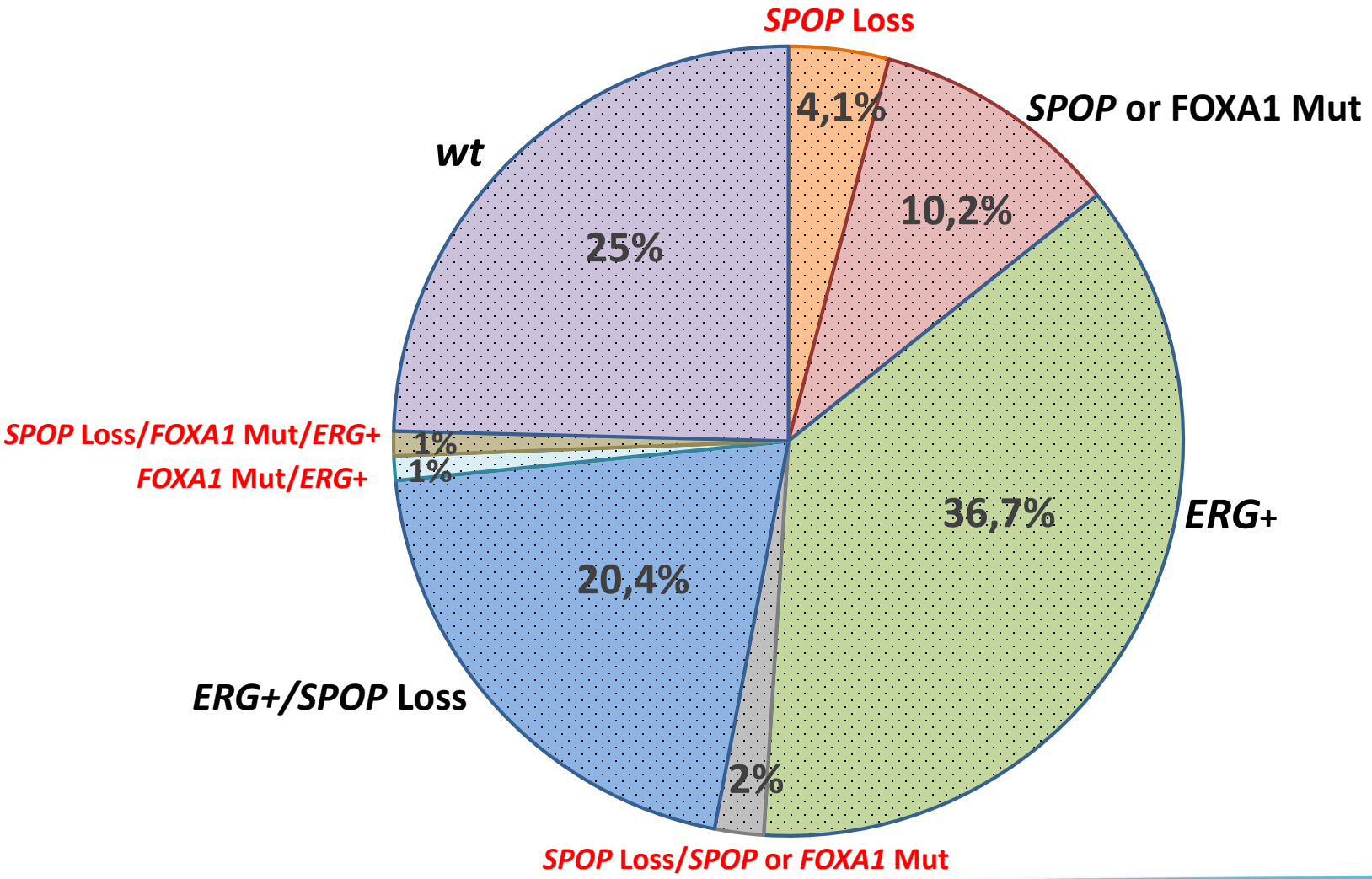
IDH1 mut 0%





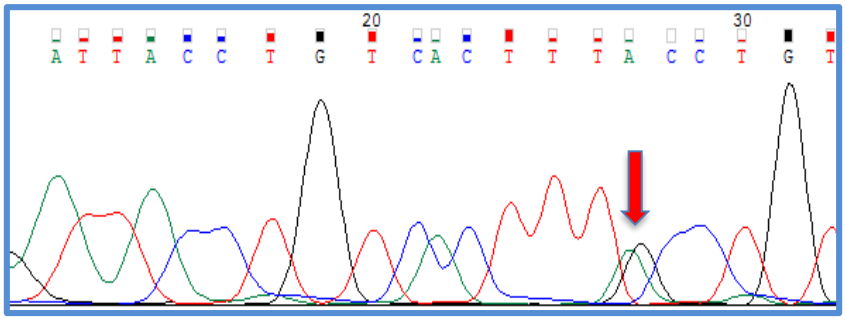


Different combinations of *SPOP, FOXA1* and *ERG* alterations in prostate cancer

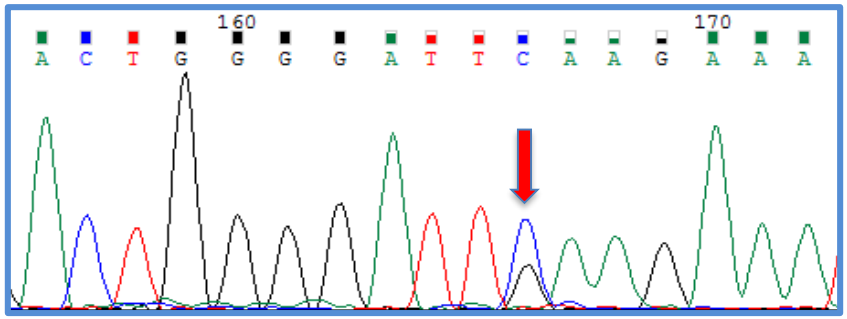


SPOP and *FOXA1* mutations examples

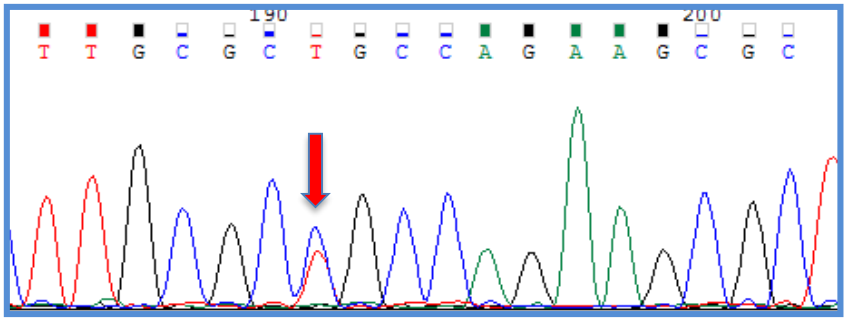
#Case 181
***SPOP* (A>G) Y87C**



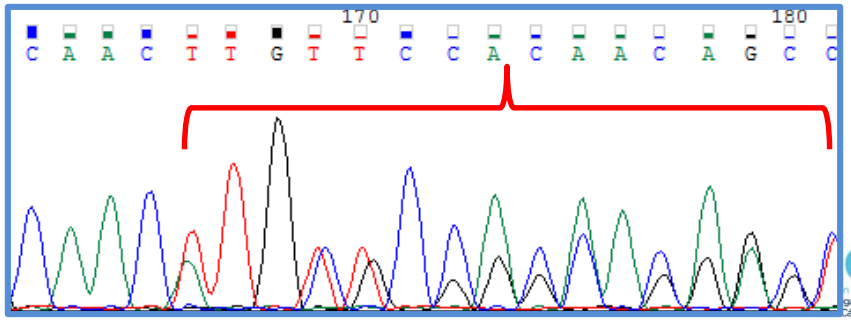
#Case 183
***SPOP* (C>G) F133L**



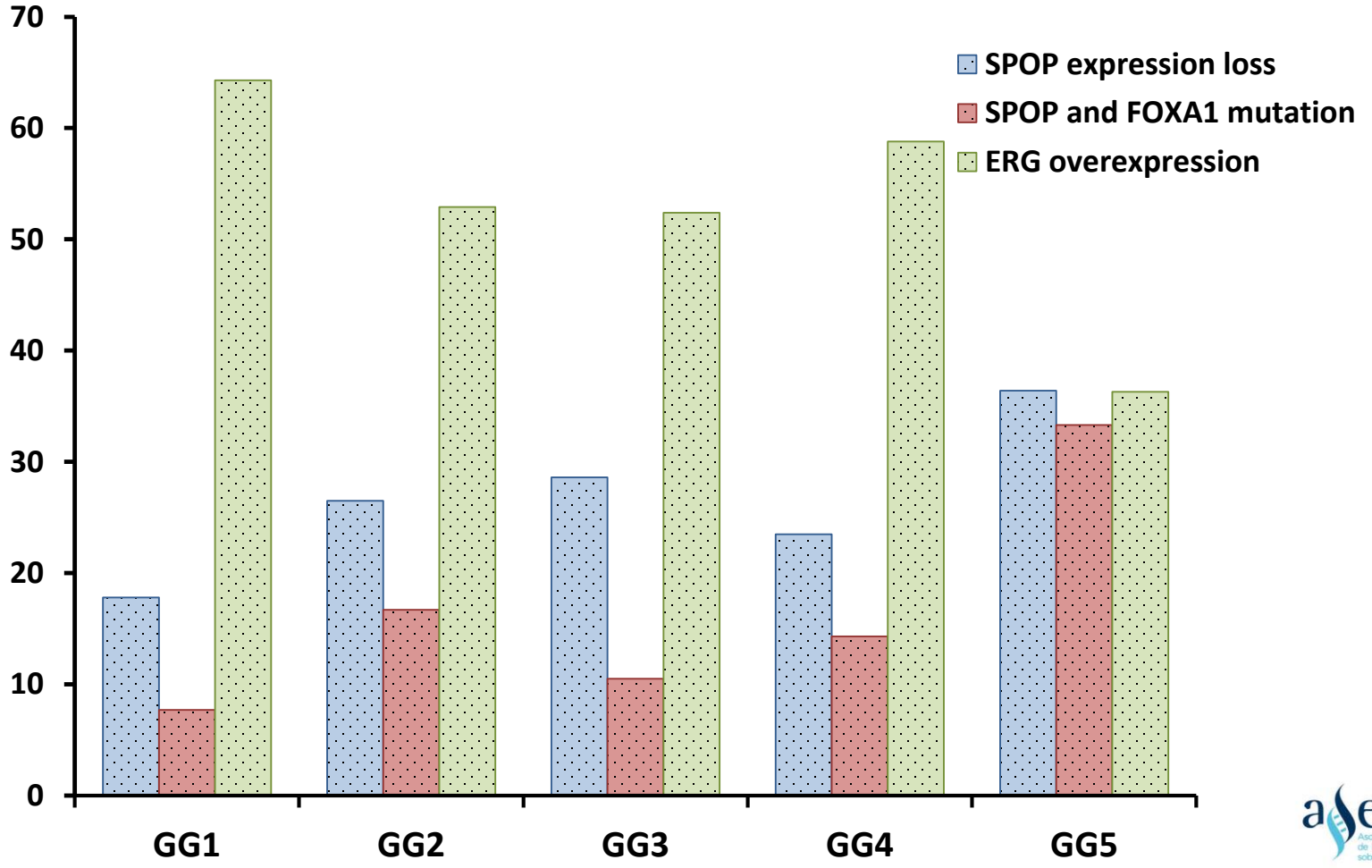
#Case 192
***FOXA1* (C>T) R262C**



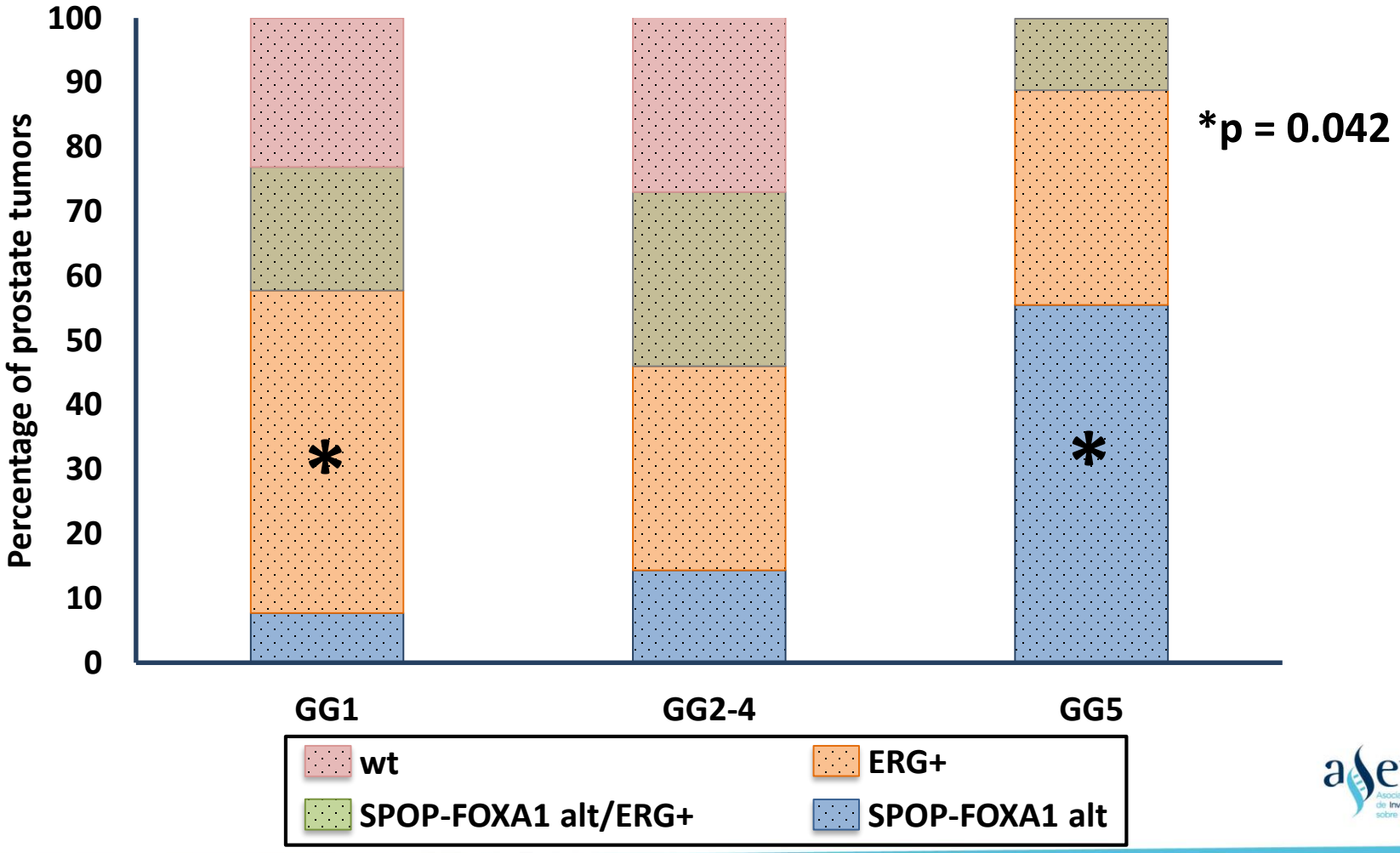
#Case 12
***FOXA1* (ins/del) M253_R261**



Distribution of *SPOP and FOXA1* alterations and *ERG* overexpression according to GG

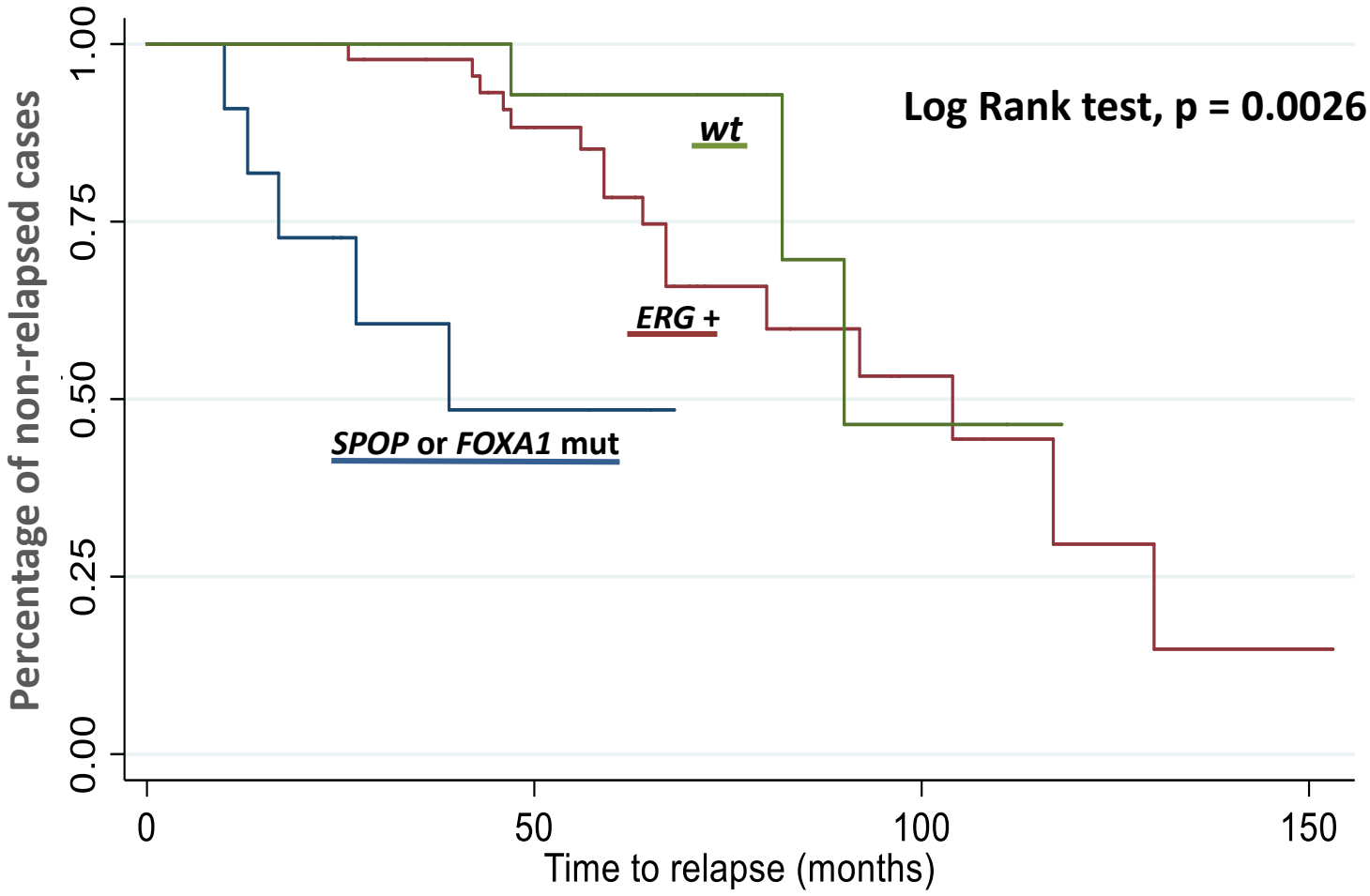


Distribution of the different combinations of alterations according to the GG



*p = 0.042

SPOP or FOXA1 mutations and biochemical (PSA) recurrence



Conclusions

SPOP expression loss characterizes a significant number of PrCa, and is statistically associated with *ERG* overexpression.

SPOP and *FOXA1* mutations show an inverse statistical correlation with *ERG* overexpression

SPOP and *FOXA1* mutations are present in a significant percentage of *ERG wt* tumors but in a very low percentage of *ERG* overexpressing tumors

SPOP and *FOXA1* alterations (expression loss and mutations) are associated with GG5 tumors, but *ERG* overexpression is associated with GG1 PrCa.

SPOP and *FOXA1* mutations are strongly associated with a shorter time of PSA recurrence in PrCa.

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