GENETIC COUNSELING IN PROSTATE CANCER

5-10% of tumors are hereditary; due to **germline mutations** in different genes that imply a **greater susceptibility** to develop cancer

GOAL

To know the **risk of prostate cancer (PCa) and other tumors** linked to hereditary cancer syndromes (HCS);
Prediction of treatment response and prognosis.
To find out the risk of HCS in his **relatives**.

WHAT ARE THE INDICATIONS? Following **Philadelphia Prostate Cancer Consensus 2019 and NCCN 2021**

- **Metastasic PCa** (included in the EAU guidelines 2021)
- **Locally advanced PCa**
- **PCa with ductal or intraductal histology** (also cribiform pattern in NCCN guidelines)
- **ISUP ≥ 4**
- **Relevant family history:** (included in the EAU guidelines 2021)
  - A first-degree or two second-degree relatives <60 years or metastasic PCa or died from PCa
  - 2 or more cases of Lynch Syndrome or hereditary breast/ovarian cancer (one relative if <50 years at diagnosis)
- **Candidates for active surveillance** (not included in NCCN guidelines)

HOW IS GENETIC COUNSELING DONE?

1. **PRE-TEST CONSULTATION**
   - Collect family health history of at least 3 generations
   - Identify the subject to study
   - Education, information, psycotheraphy
   - Discuss objectives, benefits and limitations
   - Obtain informed consent
2. **UNDERGO GENETIC TESTING (GERMLINE)**
3. **POST-TEST CONSULTATION**
   - Review the results and discuss them with the patient
   - Emotional support

It must include **at least**, the most common alterations of the 6 DNA repair genes linked to PCa:
- 4 homologous recombination repair (HR): **BRCA1, BRCA2, PLAB2, ATM**
- 2 DNA mismatch-repair (MMR): **MSH2, MSH6** and in Nordic populations include **HOXB13**

GENETIC STUDY

NEGATIVE RESULT: Same cancer risk as the general population

VARIANT OF UNCERTAIN SIGNIFICANCE (VUS): Management based on personal and/or family history

PATHOLOGICAL RESULT (2-23%)

THERAPEUTIC IMPLICATIONS

- **Worse prognosis**, more aggressiveness
- Close follow-up
- Opt for **active treatment** rather than active surveillance
- Good response to **PARP inhibitors** (HR mutation) and **pembrolizumab** (MMR mutation) in second line mCRPC
- Sequencing **1. ABI/ENZA and 2. TAXANES** seems better than vice versa

FAMILY COUNSELING

- BRCA 2: **x8** PCa risk (and more aggressive)
- BRCA 1: **x3,8** PCa risk
- MSH2, MSH6: **x2-5,8** PCa risk
- HOXB13: **x4** PCa risk (and earlier)

Genetic testing is performed **EXCLUSIVELY for the identified mutation**, not for the genetic panel

NON-CARRIER RELATIVE:
- Reassure, leave the protocol

CARRIER RELATIVE:
- Perform early screening adapted to the mutation presented

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