

Table 2. Recommendations for medical/radiation oncologists and urologists for genetic testing and counselling of patients with prostate cancer.

### Recommendations

- Genetic testing considerations should be part of routine practice as it can inform on personal and familial risk, and provides predictive and prognostic value
- Family history and informed consent should form part of routine clinical practice
- During patient selection for somatic/germline testing, the following factors should be considered:
  - Somatic testing
    - Patients with metastatic prostate cancer<sup>a</sup>
  - Germline testing
    - Age <55 years
    - Strong positive family history<sup>b</sup>
    - High-risk or very high-risk localised prostate cancer or metastatic prostate cancer regardless of family history
    - Intraductal histology
    - Patients who test positive on somatic testing for homologous recombination repair mutations
    - Ashkenazi Jewish ancestry
- Germline testing should be undertaken in patients with somatic mutations to evaluate whether the mutation is of germline origin and subsequent familial risk for patients and relatives
- In the context of available targeted therapies, somatic testing should be conducted at disease progression to metastatic castration-resistant prostate cancer, followed by germline testing to evaluate familial risk if mutations are detected
- Genetic counselling should be performed with an overall perspective on optimal disease management and potential downstream effects
- A hybrid method involving pre-test counselling prior to somatic testing conducted by the treating urologist or medical oncologist and post-test counselling (after somatic testing but prior to germline testing in indicated patients) by the genetic counsellor should be adopted in Singapore
- Urologists and medical oncologists should be appropriately trained in genetic counselling
- The distress of unexpected results should be taken into account during the counselling session

### Educational points

- Genetic testing and counselling should be discussed with the patients early in the course of the disease as patients with genetic aberrations are likely to have aggressive disease leading to an early metastatic stage that needs extensive management
- Somatic testing in particular tissue testing is considered the gold standard as it is well-established and can identify more patients with HRR mutations
- An algorithm that combines testing modalities (e.g. Fig. 1) should ensure that all meaningful pathogenic variants are identified
- Relying solely on family history of prostate cancer for conducting genetic tests may lead to missing the detection of patients, as it has been shown that 30–40% of HRR mutation carriers may not report a family history of cancer

<sup>a</sup> In patients with low- and favourable intermediate-risk localised prostate cancer and life expectancy of  $\geq 10$  years, somatic testing should be considered on a case-to-case basis according to the discretion of the healthcare professionals and patient decision.

<sup>b</sup> Family history includes high-risk germline mutations (e.g. *BRCAl/2*); brother or father or multiple family members diagnosed with prostate cancer (but not clinically localised grade group 1) at <60 years or who died from prostate cancer;  $\geq 3$  cancers on the same side of the family, especially diagnosed at age  $\leq 50$  years, bile duct, breast, colorectal, endometrial, gastric, kidney, melanoma, ovarian, pancreatic, prostate (but not clinically localised, grade group 1), small bowel or urothelial cancer