**Supplementary Table S3: Comparison of the sensitivity and specificity of different screening strategies to identify patients with UTUC related to a Lynch syndrome.**

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| --- | --- | --- | --- | --- |
| **Variables** | **Clinical risk factors for hereditary UTUC** | **MSIsensor score ≥3** | **MSIsensor score ≥10** | **TMB ≥20/Mb** |
| Number of patients in the whole cohort | 62 (31.8%) | 18 (9.3%) | 12 (6.2%) | 27 (13.8%) |
| Number of patients tested for germline mutations | 18 | 17 | 11 | 18 |
| Sensitivity | 83.3 (53.8-96.2) | 91.7 (62.1-100) | 83.3 (53.8-96.2) | 100 (71.3-100) |
| Specificity | 77.1 (60.7-88.1) | 82.9 (66.8-92.2) | 97.1 (83.9-100) | 82.9 (66.8-92.2) |
| PPV | 55.6 (32.6-78.5) | 64.7 (42.0-87.4) | 90.9 (73.9-100) | 66.7 (44.9-88.4) |
| NPV | 93.1 (83.9-100) | 96.7 (90.2-100) | 94.4 (87.0-100) | 100 |
| Number of Lynch syndromes missed | 2 | 1 | 2 | 0 |

TMB: tumor mutational burden; PPV: positive predictive value; NPV: negative predictive value.