Supplementary Table 1: Molecular docking scores (in -Kcal/mol) of TMPRSS2 protein with its selected inhibitors (ligands).

|  |  |
| --- | --- |
| **Ligand** | **Biding affinity scores** |
| Bicalutamide | -8.6 |
| Enzalutamide | -7.6 |
| Apalutamide | -8.8 |
| Flutamide | -7.3 |
| Nilutamide | -7.6 |
| Darolutamide | -7.3 |

Supplementary Table 2: Identification of the active site of TMPRSS2 protein using CASTp server.

|  |  |  |  |
| --- | --- | --- | --- |
| Pockets | Area (SA) | Volume (SA) | Amino Acid Residues |
| 1 | 307.837 | 226.012 | ASP 144, GLU 145, ASN 146, **ARG 147**, CYS 148, **VAL 149**, TYR 161, SER 163, ASP 187, **MET 188**, ASP 220, ILE 221, TYR 222, LYS 223, PRO 367, ASN 368, PRO 369, GLY 370, MET 371, MET 372, LEU 373, GLN 374, GLN 377, LEU 404, THR 447, LYS 449, **TRP 454**, ILE 456, MET 478 |
| 2 | 231.239 | 179.930 | TRP 176, ASN 179, TYR 180, **ARG 182**, ALA 183, ARG 186, ASP 187, LEU 212, ALA 216, GLY 217, VAL 219, ASP 220, TYR 222, LEU 225, ASP 482, TYR 485, ARG 486, ARG 489 |

Supplementary Table 3: Drug likeness results of the six studied ligands.

|  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- |
| S. No | Compounds | Lipinski | Ghose | Veber | Egan | Muegge | Bioavailability score |
| 1 | Bicalutamide | Yes | Yes | Yes | Yes | Yes | 0.55 |
| 2 | Enzalutamide | Yes | Yes | Yes | Yes | Yes | 0.55 |
| 3 | Apalutamide | Yes | Yes | Yes | Yes | Yes | 0.55 |
| 4 | Flutamide | Yes | Yes | Yes | Yes | Yes | 0.55 |
| 5 | Nilutamide | Yes | Yes | Yes | Yes | Yes | 0.55 |
| 6 | Darolutamide | Yes | Yes | Yes | Yes | Yes | 0.55 |

Supplementary Table 4: pharmacokinetic parameters of the six tested compounds.

|  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- |
| Pharmacokinetic properties | Compounds | | | | | |
| Bicalutamide | Enzalutamide | Apalutamide | Flutamide | Nilutamide | Darolutamide |
| Absorption | | | | | | |
| Water solubility (log mol/L) | -5.009 | -5.755 | -5.208 | -4.655 | -4.171 | -2.633 |
| Intestinal absorption (human) (% Absorbed) | 77.815 | 90.153 | 92.396 | 87.749 | 87.504 | 77.979 |
| Distribution | | | | | | |
| Blood-Brain Barrier (BBB) (log BB) | -1.154 | -1.074 | -1.284 | -0.539 | -0.732 | -1.237 |
| Metabolism | | | | | | |
| CYP2D6 substrate (Categorical Yes/No) | No | No | No | No | No | No |
| CYP3A4 substrate (Categorical Yes/No) | No | Yes | No | No | No | No |
| CYP1A2 inhibitor (Categorical Yes/No) | No | No | No | No | Yes | No |
| CYP2C19 inhibitor (Categorical Yes/No) | Yes | Yes | Yes | Yes | Yes | No |
| CYP2C9 inhibitor (Categorical Yes/No) | Yes | Yes | Yes | Yes | No | Yes |
| CYP2D6 inhibitor (Categorical Yes/No) | No | No | No | No | No | No |
| CYP3A4 inhibitor (Categorical Yes/No) | Yes | Yes | Yes | Yes | No | Yes |
| Excretion | | | | | | |
| Total Clearance (log ml/min/Kg) | 0.499 | -0.226 | -0.241 | 0.059 | 0.259 | 0.331 |
| Toxicity | | | | | |  |
| AMES toxicity (Categorical Yes/No) | No | No | No | No | Yes | No |
| Synthetic accessibility | 3.53 | 3.17 | 3.88 | 2.05 | 2.33 | 3.86 |