Hormonal clusters of testicular cancers

#3

Gonadotropin (CGA)

signaling

metabolism

hormone turnover

GRID2 deletion

TKI inhibitors

12q15 amplification

(MDM2, PTPRR, PTPRB)

High deletion count, high MSI

Hypoxia, AP1/JUN and ER-

supporession of oxidative energy

Lipid metabolism, female steroid

responsive transcriptome,

#4

EGFR, FGFR, and ER signaling

CREB and POU5F1 transcriptome,

Steroid and androgen production

No strong genetic features

cytotoxic drugs, TKI inhibitors

RNA turonver, nucleotide metabolism

#2

| Sex hormone-related gene expression | (GNRH1, PRL) Testosterone - DHT conversion (SRD5A1) Receptors: FSHR, AR Expression of ER-responsive genes | Testosterone - DHT conversion (<i>SRD5A3</i>) Receptors: <i>ESR2</i> , <i>AR</i> Expression of AR responsive genes | Estrogen/estradiol synthesis (HSD17B1, HSD18B12, CYP19A1) Sex hormone transport (SHBG) Receptors: FSHR Expression of ER-responsive genes | Steroid synthesis (STAR, POMC, HSD3B2, CYP11A1, CYP17A1) Testosterone synthesis (HSD17B3) Receptors: LHCGR, ESR2, AR |
|--|--|---|---|--|
| Histology | NSGCT, teratoma, mixed | Seminoma | NSGCT, embryonal carcinoma, mixed, yolk sac | NSGCT, embronal carcinoma, mixed, seminoma, yolk sac |
| Risk profile and prognosis | Younger patients Serum markers: S1/S2 Cancer marker expression: AFP Progression/relapse: intermediate - high risk | Older patients Serum markers: mostly S0/S1 Cancer marker expression: <i>LDHC</i> Progression/relapse: low risk | Older patients Serum markers: mostly S2 Cancer marker expression: LDHA, AFP, CGA Progression/relapse: high risk | Younger patients Serum markers: mostly S0/S1 Cancer marker expression: LDHA, AFP Progression/relapse: intermediate risk |
| Immunity, TME, ECM, and epithelial phenotype | Fibroblast-rich, immune desert Collagens, glycoproteins, and proteoglycans Keratins, mesenchymal cell features | T and B cell infiltration, immune checkpoint gene and cancer testis antigen expression ECM desert Cell adhesion | Fibroblasts, immune desert ECM regulators, fibrinogens, proteases, and protease inhibitors Mesenchymal cell features | Stroma- and immune desert ECM secreted factors |
| | FGFR, ERBB, EPH. | | FGFR, ERBB, WNT, and SRC/YAP | |

KIT and KRAS mutations

BCL2 family-,

drugs

Low deletion count, low MSI

cytoskeleton/microtubule-,

epigenetic-interfering, and DNA-toxic

proteoglycans Keratins, mesenchymal cell features ECM desert Cell adhesion FGFR, ERBB, EPH, TGF/BMP/SMAD, and SRC-YAP signaling Hypoxia, suppression of oxidative energy metabolism Nucleotide interconversion ECM desert Cell adhesion JAK/STAT and c-Kit signaling Antigen processing, inflammation, apoptosis, DNA repair Transport reactions

arachidonic acid metabolism

Genetics

Predicted drug

sensitivity

GRID2 and PDE4D gene deletions

20q11 amplification (BCL2L1, ID1)

High deletion count, high MSI

TKI inhibitors

#1

Pituitary hormone-related genes

(GNRH1, PRL)