# SnapShot: Breast Cancer
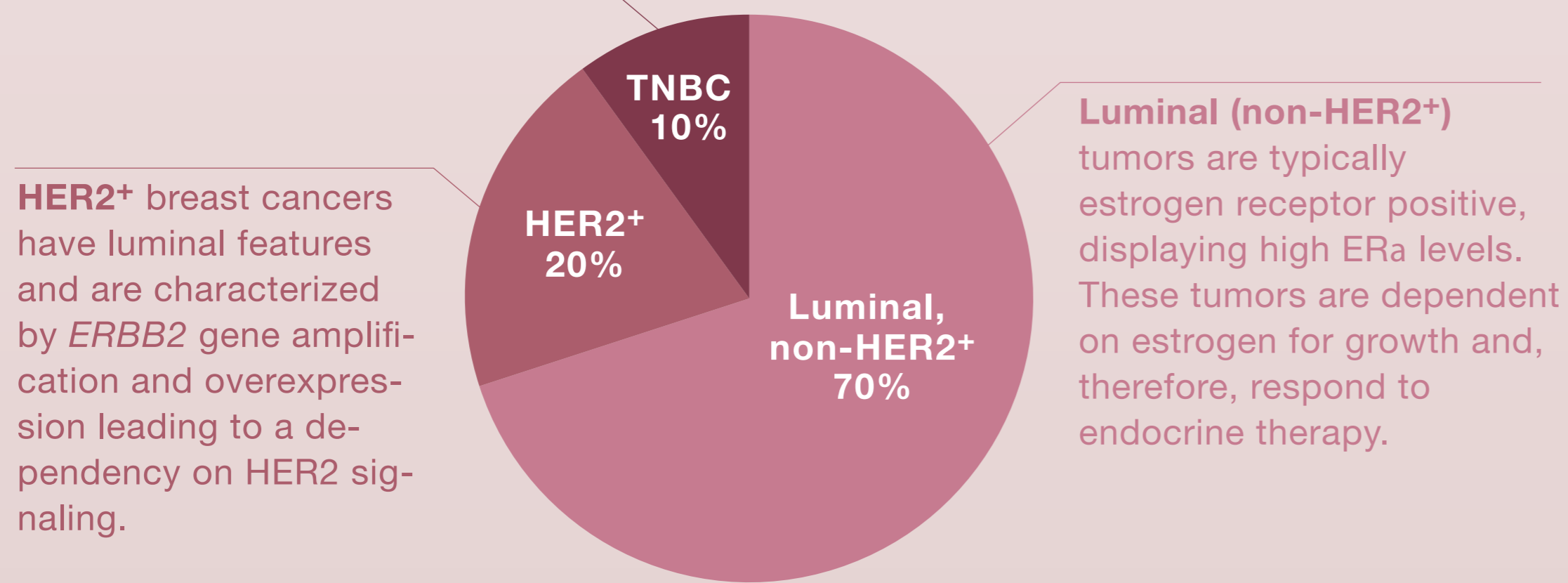
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**Cancer Cell**

## Frequency of breast cancer subtypes

**TNBC** Triple-negative breast cancers are ER⁻PR⁻HER2⁻ and show significant, but not complete, overlap with the basal-like subtype of breast cancer (which is defined by differentiation state and gene expression profile).
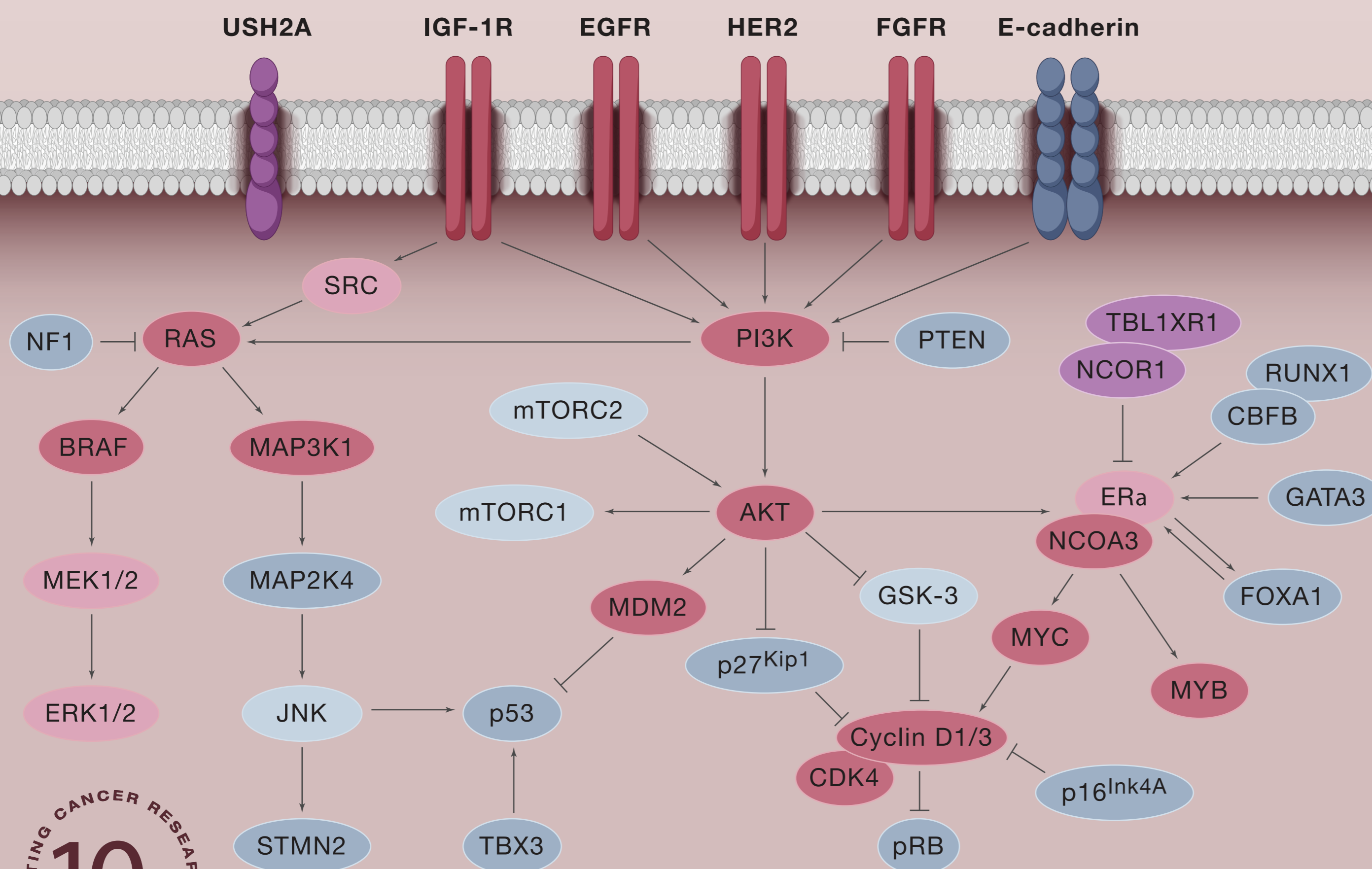
**HER2⁺** breast cancers have luminal features and are characterized by *ERBB2* gene amplification and overexpression leading to a dependency on HER2 signaling.

**Luminal (non-HER2⁺)** tumors are typically estrogen receptor positive, displaying high ERa levels. These tumors are dependent on estrogen for growth and, therefore, respond to endocrine therapy.



Pie chart: TNBC 10%, HER2⁺ 20%, Luminal, non-HER2⁺ 70%

| Subtype | Stage | 5 year OS (%) | 10 year OS (%) |
|---|---|---|---|
| *DCIS | 0 | 99 | 98 |
| Luminal (non-HER2⁺) | I | 98 | 95 |
| | II | 91 | 81 |
| | III | 72 | 54 |
| | IV | 33 | 17 |
| **HER2⁺ | I | 98 | 95 |
| | II | 92 | 86 |
| | III | 85 | 75 |
| | IV | 40 | 15 |
| TNBC | I | 93 | 90 |
| | II | 76 | 70 |
| | III | 45 | 37 |
| | IV | 15 | 11 |

*Preinvasive stage
**Estimated overall survival (OS) using HER2-targeted therapies

## Key signaling pathways in breast cancer based on somatic mutation data



Colors indicate tumor suppressors (blue), oncogenes (red), or mutant genes with unclear roles (purple), and lighter shading marks pathway components in which somatic mutations have not been identified.

### Top 21 most commonly mutated genes in breast cancer

| Gene | All (%) | Luminal | TNBC |
|---|---|---|---|
| *TP53* | 35 | 26 | 54 |
| *PIK3CA* | 34 | 44 | 8 |
| *GATA3* | 9 | 13 | 0 |
| *MAP3K1* | 8 | 11 | 0 |
| *MLL3* | 6 | 8 | 3 |
| *CDH1* | 6 | 8 | 2 |
| *USH2A* | 5 | 4 | 8 |
| *PTEN* | 3 | 3 | 3 |
| *RUNX1* | 3 | 4 | 0 |
| *MAP2K4* | 3 | 4 | 1 |
| *NCOR1* | 3 | 3 | 1 |
| *RB1* | 3 | 2 | 5 |
| *TBX3* | 2 | 3 | 1 |
| *PIK3R1* | 2 | 3 | 2 |
| *CTCF* | 2 | 2 | 1 |
| *NF1* | 2 | 2 | 1 |
| *SF3B1* | 2 | 2 | 0 |
| *AKT1* | 2 | 2 | 0 |
| *CBFB* | 1 | 2 | 1 |
| *FOXA1* | 1 | 1 | 1 |
| *CDKN1B* | 1 | 1 | 0 |

Mutation frequencies (%) in all tumors, or just within luminal (including HER2⁺) and TNBC subtypes.

| ER | HER2 | PI3K Pathway (PI3K, AKT, mTOR) | | IGF, IGF-1R | Angiogenesis (VEGFR, PDGFR, KIT) | | PARP | Others (Target) |
|---|---|---|---|---|---|---|---|---|
| Anastrozole | Afatinib | AZD8055[b] | INK1117 | BMS-754807 | Aflibercept | Olaratumab | BMN-673 | Cabozantinib[e], Foretinib[e], Onartuzumab (MET) |
| Estradiol | Canertinib | BEZ235[c] | INK128[b] | Cixutumumab | Axitinib | Pazopanib | CEP-9722 | |
| Exemestane | Dacomitinib | BGT226 | MK2206[b] | Dalotuzumab | Bevacizumab | Ponatinib | E7016 | AZD4547, BGJ398, Dovitinib, E-3810[e], HGS1036 (FGFR) |
| Fulvestrant | Lapatinib | BKM120 | PF-04691502[c] | Figitumumab | Brivanib | Sorafenib | INO-1001 | |
| Megestrol | MM-121 | BYL719 | PKI-587[c] | Ganitumab | Lenvatinib | Sunitinib | MK4827 | AUY922, Retaspimycin, Tanespimycin (HSP90) |
| Letrozole | Neratinib | Everolimus[b] | PX-866 | Linsitinib | MEDI-575 | Semaxanib | Olaparib | |
| Raloxifene[a] | Pertuzumab | GDC-0032 | Temsirolimus[b] | MEDI-573 | Motesanib | Vandetanib | Rucaparib | Ruxolitinib (JAK) |
| Tamoxifen | Trastuzumab | GDC-0068[d] | XL147 | | Nintedanib | Vatalanib | Veliparib | Denosumab (RANKL) |
| Toremifene | T-DM1 | GDC-0941 | XL765[c] | | | | | |
| | | GDC-0980[c] | | | | | | |

[a] Raloxifene is used for breast cancer prevention, not treatment, [b] mTOR inhibitor, [c] dual PI3K/mTOR inhibitor, [d] AKT inhibitor, [e] also inhibits VEGFR.

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