

## THYM - Thymoma

Subtype (WHO histology)	Biology & Expression	Genomic Alterations	Clinical Features
<b>B-like (Subtype 1)</b> (mostly B1– B3)	<ul style="list-style-type: none"> <li>• High lymphocyte infiltration (“immune-hot”)</li> <li>• Enrichment of immune/inflammatory programs</li> <li>• Down-regulated p53 signaling; up-regulated MYC/E2F pathways</li> </ul>	<ul style="list-style-type: none"> <li>• Very low TMB; few recurrent point mutations</li> <li>• Arm-level copy-number gains/losses enriched in B2/B3 tumors</li> </ul>	<ul style="list-style-type: none"> <li>• Intermediate prognosis</li> <li>• Strongly associated with myasthenia gravis</li> <li>• Standard surgical ± radiation management</li> </ul>
<b>TC-like (Subtype 2)</b> (thymic carcinoma)	<ul style="list-style-type: none"> <li>• Epithelial carcinoma-like profile; “immune-cold”</li> <li>• Down-regulated p53; up-regulated MYC/E2F and proliferation pathways</li> </ul>	<ul style="list-style-type: none"> <li>• High burden of arm-level CNAs</li> <li>• Frequent loss of chr 16q and TP53 alterations</li> <li>• Elevated TMB (including occasional MSI)</li> </ul>	<ul style="list-style-type: none"> <li>• Worst overall survival</li> <li>• Aggressive, often advanced-stage at presentation</li> <li>• Poorly responsive to conventional therapies</li> </ul>
<b>AB-like (Subtype 3)</b> (mostly AB)	<ul style="list-style-type: none"> <li>• Mixed epithelial/lymphoid profile; “immune-hot”</li> <li>• Down-regulated p53; up-regulated oncogenes (MYC/E2F)</li> <li>• Overexpression of chr 19q13.42 miRNA cluster</li> </ul>	<ul style="list-style-type: none"> <li>• High frequency of GTF2I L424H mutations</li> <li>• Low CNA burden; very low TMB</li> </ul>	<ul style="list-style-type: none"> <li>• Intermediate prognosis</li> <li>• Frequently associated with myasthenia gravis</li> <li>• PI3K/AKT activation suggests potential targeted options</li> </ul>
<b>A-like (Subtype 4)</b> (A ± AB)	<ul style="list-style-type: none"> <li>• Spindle epithelial-like (“A-type”) profile; “immune-cold”</li> <li>• Up-regulated p53 signaling; down-regulated MYC/E2F and proliferation pathways</li> </ul>	<ul style="list-style-type: none"> <li>• GTF2I L424H mutations common</li> <li>• Occasional HRAS activating mutations</li> <li>• Low CNA burden; very low TMB</li> </ul>	<ul style="list-style-type: none"> <li>• Best prognosis among subtypes</li> <li>• Rare myasthenia gravis</li> <li>• Highly chemo-/radiosensitive; GTF2I offers a potential therapeutic target</li> </ul>