Thymosin Alpha-1 (TA1) — Basic Review Questions

1. What is Thymosin Alpha-1 (TA1), what type of peptide is it, and what is its regulatory status?

Answer: Thymosin Alpha-1 (TA1, trade name Thymalfasin/ZADAXIN) is a 28-amino acid immunomodulatory peptide originally derived from the thymus — the gland that trains the immune system's T cells. It is given by subcutaneous injection. It is the most clinically established peptide in this series: approved in more than 35 countries for hepatitis B and C, though it is not FDA-approved in the US, where all use is investigational and off-label.

2. How does TA1 work, and why is it called a modulator rather than a stimulant?

Answer: It acts mainly through Toll-like receptors (especially TLR2 and TLR9) on immune cells, restoring balanced immune function rather than just revving everything up. It strengthens the antiviral and antitumor side of immunity (boosting Th1 responses, CD8 "killer" T cells, NK cells, and dendritic cells) while at the same time calming excess inflammation (lowering TNF-α and IL-1β, raising the anti-inflammatory IL-10). That two-way, homeostasis-restoring action is why it is described as a modulator, not a blunt stimulant — and it is also a key reason it is so well tolerated.

3. What is the main clinical use, and who benefits most?

Answer: Its established use is chronic hepatitis B and C, but its strongest practical role is as targeted immune rescue in people whose immune system is depleted or "paralyzed" — for example, lymphopenic viral illness, sepsis with immune exhaustion, and immune support in the elderly or dialysis patients. Benefit is greatest in patients with low lymphocyte counts, and validated thresholds (such as CD8+ below 400 or CD4+ below 650) help identify strong candidates. It is best deployed as a targeted rescue in the immunosuppressed, not as a general "booster" for healthy people.

4. How does TA1 compare with LL-37, the other immune-regulation peptide?

Answer: Both regulate immunity rather than simply switching it on or off, but they work at different points. LL-37 is the body's antimicrobial peptide — it directly kills microbes and shapes the local innate-immune response (and is gated by vitamin D). TA1 works more centrally on the adaptive immune system, restoring T-cell function and balance through Toll-like receptors. They also differ sharply in evidence: LL-37 is largely preclinical, whereas TA1 has genuine human data — Phase III trials and large meta-analyses — making it the more clinically validated of the two.

5. What does the human evidence show?

Answer: Unusually for this series, the human evidence is strong and quantified. There are Phase III randomized trials in hepatitis B, a meta-analysis of 19 sepsis trials showing roughly a 41% reduction in 28-day mortality, COVID-19 studies showing reduced mortality (about 30% down to 11% in one severe-illness cohort), and a large lung-cancer (NSCLC) analysis where TA1 improved disease-free and overall survival. Two practical patterns emerge: in viral illness it works best given early and frequently in

the first days, and as a cancer adjuvant the benefit grows with long courses (greater than 24 months).

6. What are the main cautions and the safety profile?

Answer: TA1 has an exceptional safety record — across the trials reviewed, the main side effect was mild, transient injection-site reactions, with no significant systemic adverse events, no hepatotoxicity, and no treatment discontinuations even at high sepsis doses. The cautions are mechanistically logical: because it enhances immune activity, it should be avoided in transplant patients on immunosuppression (it may work against their regimen), during an active autoimmune flare (theoretical risk of worsening), and in primary immune deficiency (no expected benefit). It is adjunctive — not a replacement for standard antiviral or antibiotic therapy. The honest limitation is the lack of large Western Phase III trials and an unclear US regulatory path.