Incorporation of SKI-G-801, novel AXL inhibitor, with anti-PD-1 inhibitor plus chemotherapy improved anti-tumor activity and survival outcome via enhancing anti-tumor T cell immunity

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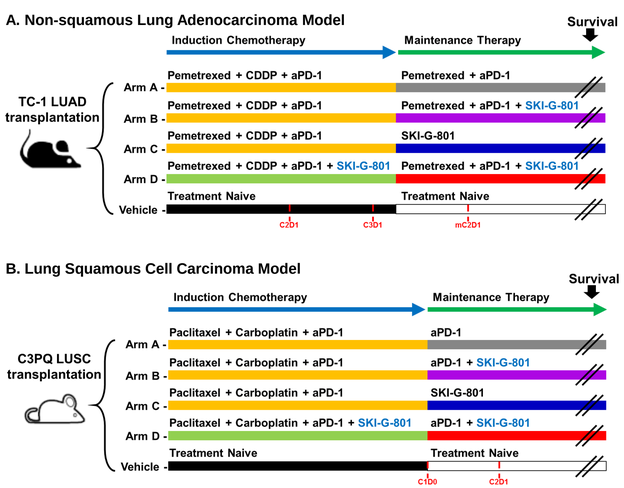
Background

AXL has been identified to play multiple roles in the tumor microenvironment including the promotion of epithelial-mesenchymal transition and immune evasion. SKI-G-801, a small molecule inhibitor targeting phosphorylation of AXL, presented strong inhibition of cancer migration and invasion. Anti-PD-1 inhibitor (αPD-1) combined with paclitaxel/carboplatin and pemetrexed/cisplatin are standard therapy in non-squamous and squamous lung cancer patients, respectively. Herein, we present that adding AXL inhibition with SKI-G-801 on αPD-1 plus chemotherapy suppressed tumor growth and improved overall survival and also enhanced anti-tumor T cell immunity in both non-squamous and squamous lung cancer models.

Syngeneic model design



Results

Figure 1 The combination effect with SKI-G-801 in TC1 non-squamous lung adenocarcinoma model

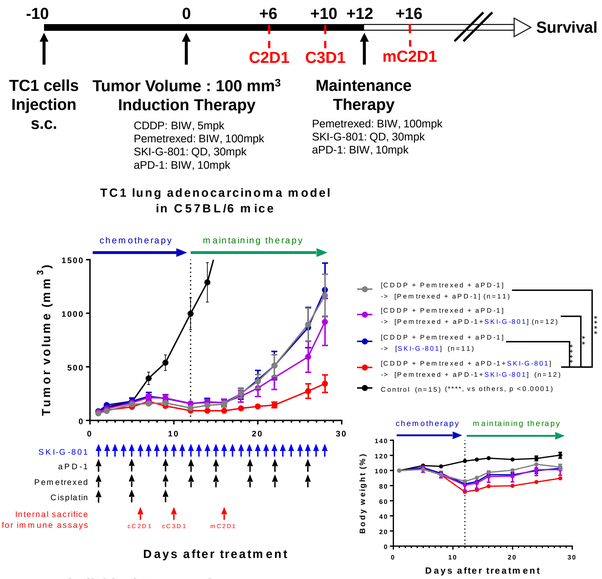


Figure 2 The combination effect with SKI-G-801 in C3PQ lung squamous cell carcinoma model

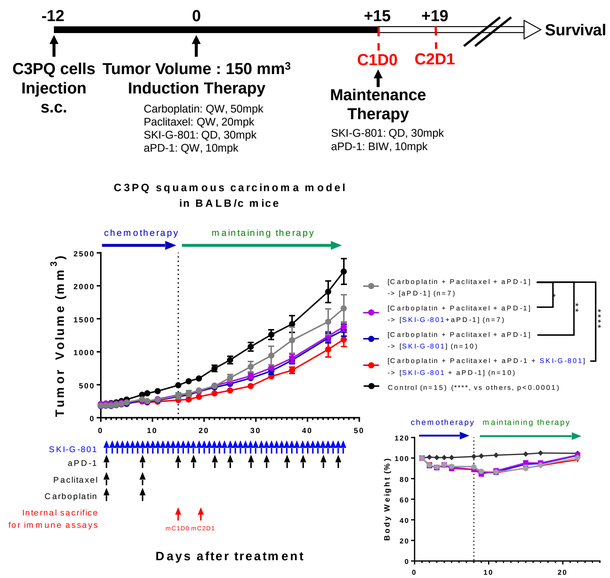
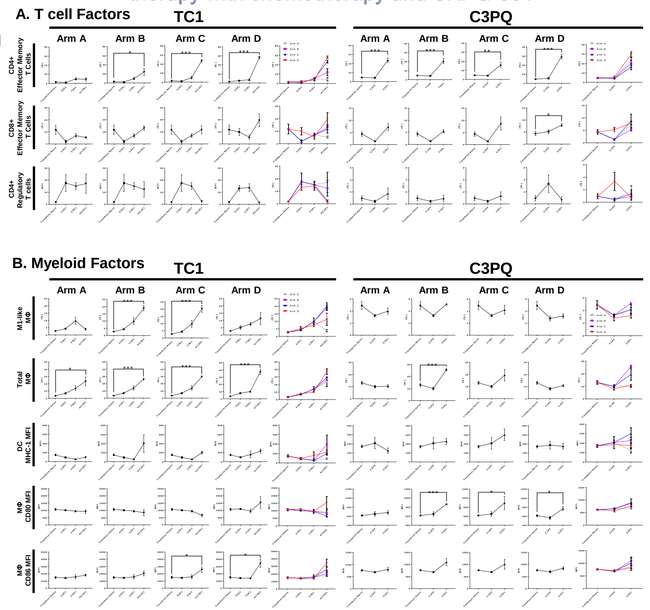
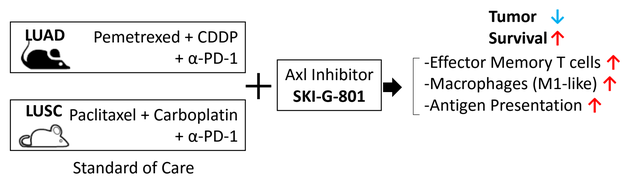


Figure 3 The immune phenotype changes of combination therapy with chemotherapy and SKI-G-801



Conclusion

Incorporation of SKI-G-801, a novel AXL inhibitor, with αPD-1 combined with chemotherapy (Standard of care) significantly improved overall survival and anti-tumor activity in both non-squamous and squamous lung cancer model through enhancing cytotoxicity of CD8+ T cells and memory CD4+ T cells. These findings provide mechanistic insight into the activity of SKI-G-801 combined with standard therapy and support its clinical development in metastatic NSCLC as first line therapy.



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