Preclinical and bioinformatics analyses were conducted to identify a target for phase 1 clinical testing of LYC-55716. LYC-55716 is a first-in-class, oral, small-molecule investigational agent that selectively activates RORγt. This master transcription factor is responsible for type 17 effector T cell differentiation and function. Clinical phase 1 testing of LYC-55716 evaluated a low percentage of BC patients expressing high levels of RORγt. These translational and bioinformatics studies of RORγt biology suggest BC and BC are likely to respond to RORγt agonist therapy. These studies have shown a positive correlation between immunotherapeutic efficacy and infiltration of T cells (eg, CD3a, CD4, CD8) in bladder cancer. A literature review also indicated that IL-17 is implicated in the efficacy of Bacillus Calmette-Guérin immunotherapy for bladder cancer.

**TARGET BIOLOGY**

Certain sterols can function as RORγt ligands and partially activate RORγt, but sterol levels are likely low in exhausted immune cells. These translational and bioinformatics studies of RORγt biology suggest RCC and BC are likely to respond to RORγt agonist therapy.

**METHODS**

Bioinformatic analyses were conducted using data on patients with RCC and BC from The Cancer Genome Atlas (TCGA). The resulting dataset was evaluated for Figure 1A. Expression of RORγt and RORγt-inducing cytokines; Steroid genes associated with RORγt (corticosteroids) and anti-RORγt (steroids) agents; correlation with patient survival (Figure 3).

**IMMUNE PROFILE**

Studies have shown a positive correlation between immunotherapeutic efficacy and infiltration of T cells (eg, CD3a, CD4, CD8) in bladder cancer. A literature review also indicated that IL-17 is implicated in the efficacy of Bacillus Calmette-Guérin immunotherapy for bladder cancer.

**RESULTS**

Analysis revealed a positive correlation between patient survival and expression of RORγt (or the RORγt signature gene IL17A). IL17A expression is associated with better survival in patients with RCC, KICH, and KIRP.

**REFERENCES**

5. Available at: https://www.asco.org/download/asi/Photo/Download/Oncoimmunology.pdf
6. Available from: ASCO® and the author of this poster. Code are for personal use only and may not be reproduced without permission from ASCO®.

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**CONCLUSIONS**

- RORγt agonist LYC-55716 is a novel immuno-oncology agent that effectively activates RORγt and expression of RORγt agonist further enhances immunotherapeutic efficacy and patient survival.
- These preclinical and bioinformatics studies of RORγt biology support the inclusion of RCC and BC (Urothelial carcinoma) patients in an ongoing 2a Expansion trial of LYC-55716 (Table 1).