a novel mouse model of APS3v. The APS3v mouse model was established by immunizing humanized NOD-DR3 mice with Tg.1571, TPO.758 and GAD.492 combined, together with adjuvant. We then validated hit small molecules for their effectiveness in blocking stimulation of T-cell responses in the APS3v mouse model. **Results:** Our screen identified 4 small molecules (S5, S9, S15, S53) that showed more than 50% inhibition in our *in vitro* assay. We were also able to establish a novel APS3v mouse model. Immunized mice showed an increase in cytokine production in response to all 3 thyroidal and islet peptides. The immunized mice also developed antibody responses against each peptide. When we tested the 4 "hit" compounds, only Cepharanthine (S53) which we previously identified as a small molecule blocking AITD immune responses, could block all 3 thyroidal/islet peptides in the APS3v mouse model. Treating with Cepharanthine prior to inducing APS3v in the mice also reduced T-cell proliferation in the immunized mice. **Conclusions:** We established a novel humanized APS3v mouse model by co-immunizing 3 thyroidal and islet peptides. We also identified Cepharanthine as a small molecule that can block thyroid and islet specific T-cell responses in this model. Cepharanthine can be further tested in APS3v patients carrying the specific APS3v-DR pocket as a potential therapeutic treatment.

Thyroid

THYROID CANCER AND AUTOIMMUNITY

Estimabl2: Is There a Need for Radioiodine Ablation in Low Risk Differentiated Thyroid Cancer (DTC) Patients?: Results From the French Randomized Phase III Prospective Trial on 776 Patients (NCT 01837745)

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Background: The benefits of post-operative radioactive iodine (RAI) administration have not been demonstrated in patients with low risk differentiated thyroid cancer (DTC). The objective of this randomized phase III trial is to assess in low risk DTC patients the non-inferiority of a follow-up strategy as compared to a systematic adjuvant post-operative RAI administration.

Methods: ESTIMABL2 is a French multicentric randomized phase III trial in patients with low-risk DTC treated with total thyroidectomy with or without prophylactic neck lymph node dissection (pT1am N0 or Nx with a sum of the diameters of tumor lesions ≥ 10mm, pT1b N0 or Nx). Two to five months after surgery, in the absence of suspicious lateral neck lymph node on ultrasonography (US), patients were randomized either to the follow-up group (FU, no RAI administration) or to the ablation group and received post-operative RAI (1.1 GBq following rhTSH stimulation). Yearly controls under levothyroxine treatment consisted in thyroglobulin (Tg) and Tg antibodies (TgAb) determinations and neck-US. The primary objective was to assess at 3 years after randomization the non-inferiority of the proportion of patients without tumor-related event in the FU group as compared to the ablation group. Non-inferiority is demonstrated if the rate of patients without event at 3 years does not differ by more than ΔL=-5%. A tumor-related event was defined by the occurrence of subsequent treatment (RAI administration or surgery) for abnormal RAI uptake on the post-therapeutic WBS or by elevated Tg or TgAb levels and/or abnormal neck US during controls. Tg levels on levothyroxine treatment were considered elevated if > 2ng/mL in the FU group and > 1ng/mL in the ablation group. TgAb were considered elevated if > the upper limit range with an increase above 50% on 2 consecutive determinations performed 6 months apart.

Results: 776 low-risk DTC patients were included between 2013 and 2017 in 35 French centers within the TUTHYREF network; 83% females, mean age: 52 years, papillary TC: 96%, pT1bNx: 43.6%, pT1bN0: 37.5%, pT1amNx: 12.6%, pT1amN0: 6.3%. Among the 729 patients evaluable at 3 years after randomization, tumor-related events occurred in 18/367 patients (4.9% IC95%=[2.9; 7.6]) in the FU group and in 15/362 patients (4.1% IC95%=[2.3; 6.7]) in the ablation group. Thus, 95.1% of patients in the FU group had no event at 3 years and this percentage is not inferior from the 95.9% of patients observed in the ablation group (difference = -0.8% [95% CI:-3.3%; 1.8%]. The number of subsequent surgery and/or RAI administration was 6 (1.6% IC95%=[0.6; 3.5]) in the FU group and 9 (2.5% IC95%=[1.1; 4.7]) in the ablation group.

Conclusion: this phase III trial demonstrates the non-inferiority of a follow-up strategy compared to a systematic adjuvant post-operative administration of RAI (1.1GBq following rhTSH) in low risk DTC patients (PHRC 2012; NCT01837745).