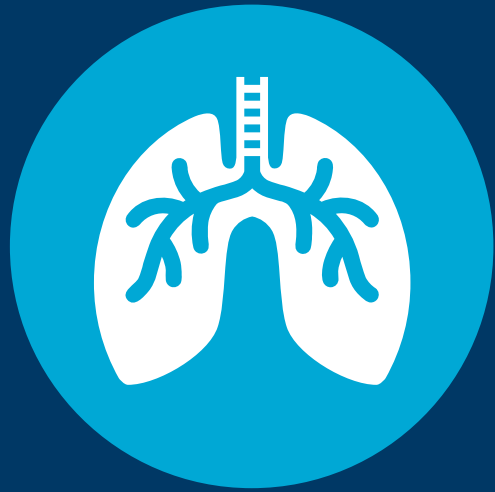




SKYSCRAPER-05: Phase II Study of Neoadjuvant Atezolizumab + Tiragolumab With or Without Platinum-Based Chemotherapy in Patients With Locally Advanced Resectable Stage II–IIIB Non-Small Cell Lung Cancer

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Current treatment options for resectable, stage II–IIIB NSCLC

- Emerging data from recent phase III studies have demonstrated that neoadjuvant or adjuvant anti-PD-L1/PD-1 agents + chemotherapy (CT) improved outcomes in patients with resectable NSCLC^{1–3}
- Despite these advances, there still remains an unmet need to further improve upon the outcomes of patients with early-stage resectable NSCLC

Rationale

- TIGIT is a novel inhibitory immune checkpoint present on activated T cells and NK cells in multiple cancers; TIGIT expression correlates with PD-1, especially in tumour-infiltrating T cells⁴
- In preclinical models, concomitant targeted inhibition of both the TIGIT and PD-1/PD-L1 pathways demonstrated superior efficacy over the respective single-agent⁴
- Tiragolumab is a first-in-class, monoclonal antibody that selectively binds to TIGIT (**Figure 1**); tiragolumab is designed to block the TIGIT pathway, which may inhibit immunosuppressive signalling and may allow the CD226 pathway to resume its T-cell-activating functions^{4–7}
- In the phase II CITYSCAPE study (NCT03563716), first-line tiragolumab + atezolizumab in PD-L1-selected (TPS ≥1%) Stage IV NSCLC resulted in a clinically meaningful improvement in ORR, PFS, and OS in the ITT population, driven by the PD-L1-high (TPS ≥50%) subgroup, compared with placebo + atezolizumab.^{8,9} Cohort A of SKYSCRAPER-05 will include only patients with tumours having PD-L1 TC ≥50% expression
- CT and radiotherapy may upregulate PD-L1 expression in the tumour^{10–12} and clinical benefit of CT combined with PD-L1/PD-1 inhibitors have been documented by improved OS and PFS in metastatic NSCLC patients throughout all PD-L1 subgroups. Cohort B of SKYSCRAPER-05 will enroll PD-L1 all-comers to receive CT + immunotherapy^{13–17}

References

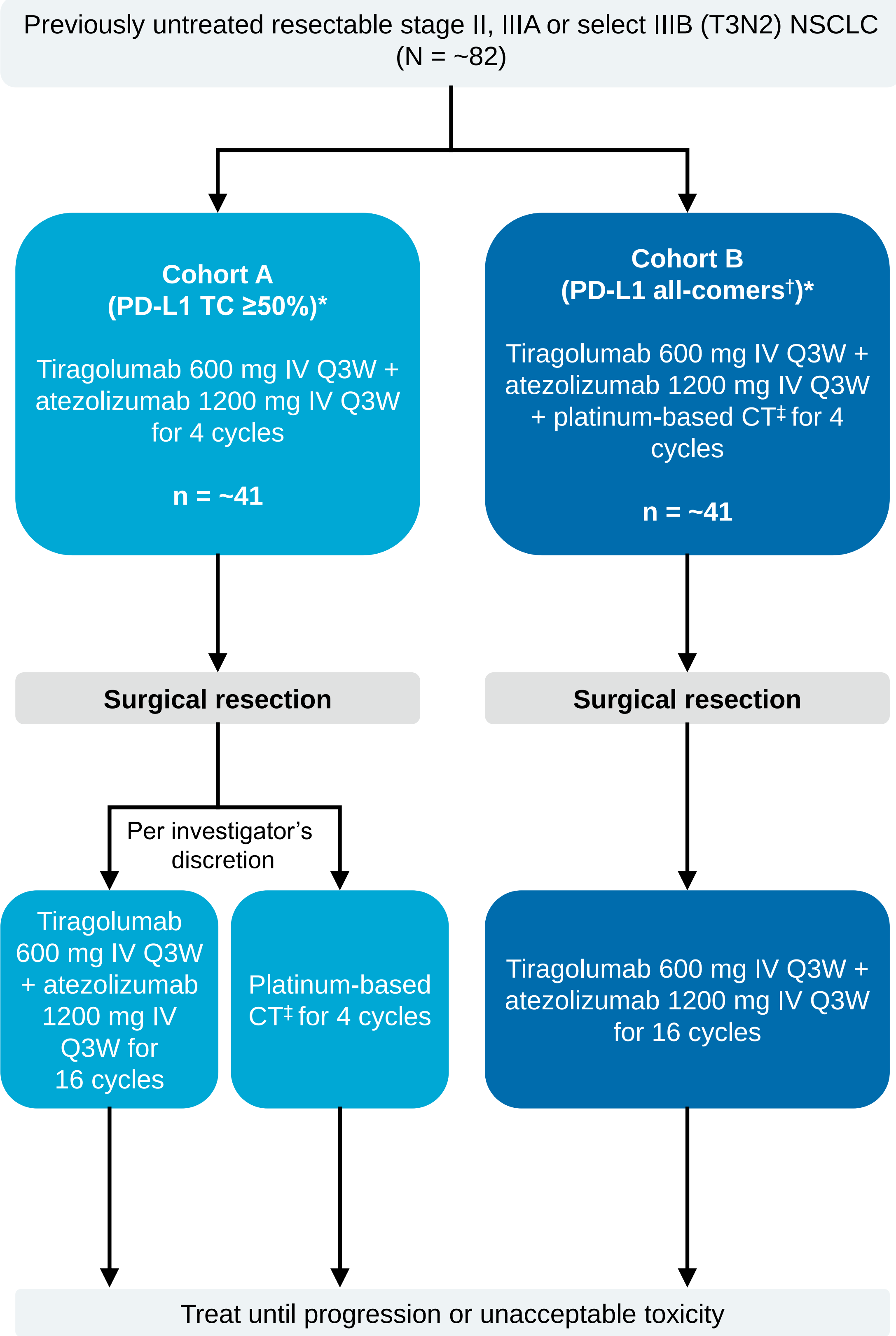
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CLINICAL TRIAL DESIGN

- SKYSCRAPER-05 (NCT04832854) is a multicenter, open-label, phase II study of atezolizumab + tiragolumab, with or without platinum-based CT, in patients with previously untreated, locally advanced, resectable NSCLC
- SKYSCRAPER-05 is a proof-of-concept study designed to investigate efficacy and safety of neoadjuvant and adjuvant tiragolumab + atezolizumab with or without CT
- The study schema for SKYSCRAPER-05 is shown in **Figure 2**
- Key eligibility criteria for SKYSCRAPER-05 are listed in **Table 1**

Figure 2: SKYSCRAPER-05 study design



*Cohort assignment by tumour specimen PD-L1 status

†Patients with any level of PD-L1

‡Chemotherapy options: cisplatin 75 mg/m² / carboplatin 5 or 6 mg/mL/min + pemetrexed 500mg/m² will be administered by IV infusion on Day 1 of each 21-day cycle (for non-squamous only); cisplatin 75 mg/m² / carboplatin 5 or 6 mg/mL/min will be administered by IV infusion on Day 1 of each 21-day cycle + gemcitabine 1000 or 1250 mg/m² will be administered by IV infusion on Days 1 and 8 of each 21-day cycle (for squamous only); carboplatin 5 or 6 mg/mL/min + paclitaxel 175 or 200 mg/m² will be administered by IV infusion on Day 1 of each 21-day cycle
CT; chemotherapy; IV, intravenous; Q3W, once every 3 weeks, TC, tumour cell

DISCLOSURES

Harvey Pass declares the following: Speaker's Bureau (Beigene, Genentech); Advisory board and advisory role (F-Hoffmann-La Roche/Genentech); financial royalties (NIH cell lines; Mesothelioma Book); research grant and funding (NCI/NIH; AACR) and steering committee roles.

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Table 1: Key eligibility criteria for SKYSCRAPER-05

Key inclusion criteria	Key exclusion criteria
✓ Age ≥18 years	× NSCLC with an activating <i>EGFR</i> mutation or <i>ALK</i> fusion oncogene
✓ ECOG PS 0–1	× NSCLC with histology of large cell neuroendocrine carcinoma, sarcomatoid carcinoma, or NSCLC not otherwise specified
✓ Histologically or cytologically confirmed Stage II, IIIA, or select IIIB (T3N2 only) NSCLC of squamous or non-squamous histology	× SCLC histology or NSCLC with any component of SCLC
✓ Eligible for R0 resection with curative intent at the time of screening	× Any prior therapy for lung cancer
✓ Eligible to receive a platinum-based CT regimen	× Active or history of autoimmune disease or immune deficiency
✓ Measurable disease, as assessed by the investigator per RECIST v1.1	× History of idiopathic pulmonary fibrosis, organizing pneumonia, drug-induced pneumonitis, idiopathic pneumonitis, or evidence of active pneumonitis on screening chest computed tomography scan
✓ Availability of a representative tumour specimen that is suitable for determination of PD-L1 status	× Prior treatment with CD127 agonists or checkpoint inhibitor therapies, including anti-CTLA-4, anti-PD-1, anti-TIGIT, and anti-PD-L1 therapeutic antibodies

CT, chemotherapy; CTLA-4, cytotoxic T-lymphocyte antigen 4; ECOG PS, Eastern Cooperative Oncology Group performance status; NSCLC, non-small cell lung cancer; PD-L1, programmed death-ligand 1; PD-1, programmed cell death protein 1; RECIST, Response Evaluation Criteria in Solid Tumours; SCLC, small cell lung cancer; TIGIT, T-cell immunoglobulin and ITIM domain



Co-primary endpoints:

Major pathological response, safety, and treatment-related surgical delays, complications and cancellations



Key secondary endpoints:

Pathological complete response and event free survival, pharmacokinetics, and immunogenicity

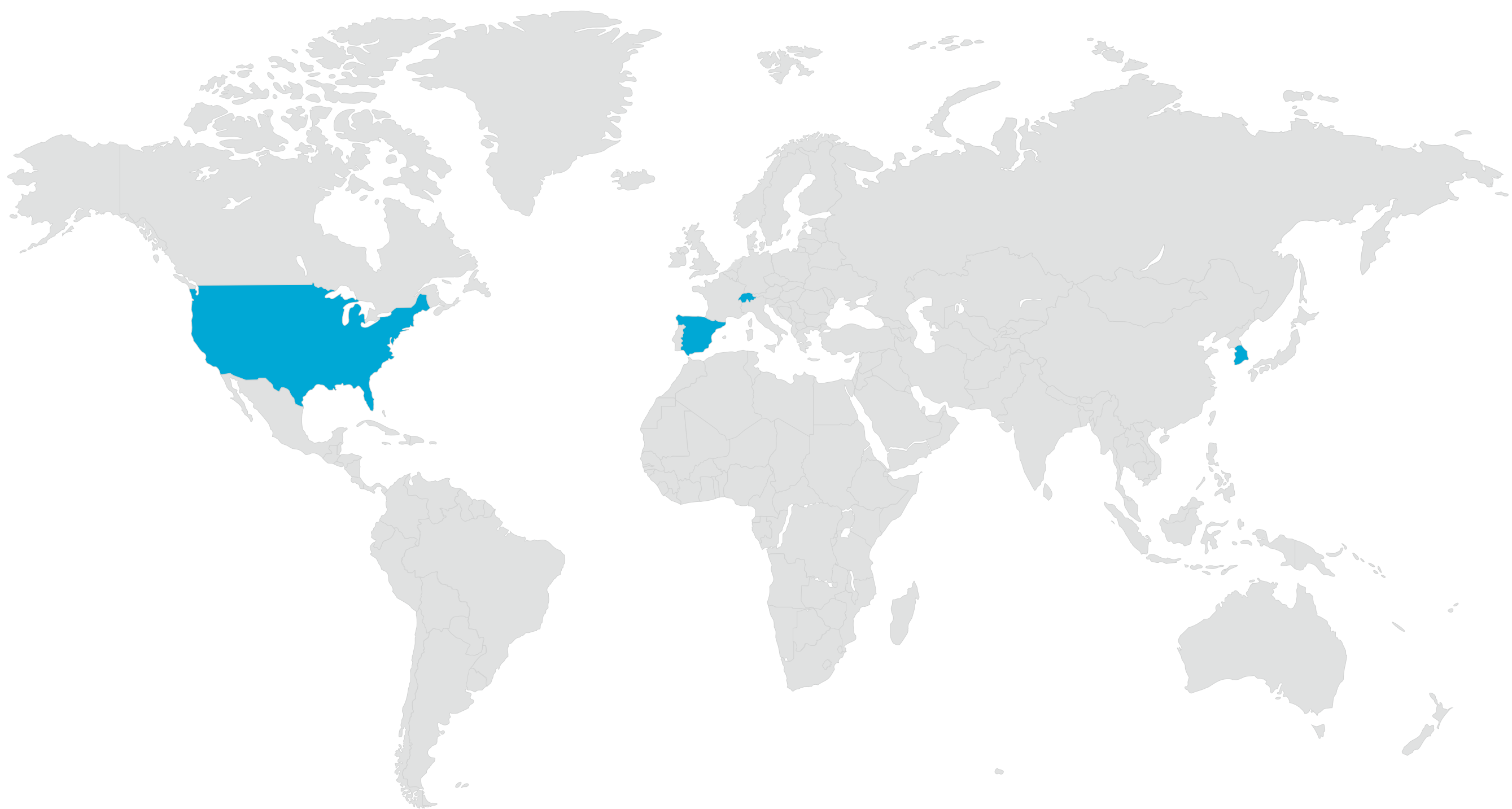


ENROLLMENT

Figure 3: Enrollment sites in SKYSCRAPER-05

- Approximately 82 participants will be recruited into the SKYSCRAPER-05 study at approximately 24 sites globally (**Figure 3**); enrollment is currently ongoing in the following countries:

- Republic of Korea
- Spain
- Switzerland
- United States



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FURTHER INFORMATION

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