NOVARTIS

IIT US Areas of Interest

Oncology

Tisagenlecleucel (Kymriah)

- Essential factors for selecting patients for Kymriah (tisagenlecleucel) therapy to improve safety and/or response for their approved indications
- Essential factors for sequencing Kymriah (tisagenlecleucel) therapy with other therapies and determining outcomes for their approved indications
- Novel combinations of therapies with Kymriah (tisagenlecleucel) to improve response and/or safety for their approved indications
- Study outcomes of Kymriah (tisagenlecleucel) administered at various sites (e.g., in-patient, out-patient, community hospital, community practice) for their approved indications

Asciminib (Scemblix)

CML-CP in Earlier Lines (1L & 2L)

- Sequencing of TKIs, clinical efficacy, and safety in real-world setting
- Patient – reported outcomes (PROs) and Quality of life issues with current CML therapies
- Biomarkers for TFR and safety
- Long-term safety and tolerability
- Studies aiming to improve the eligibility to attempt TFR and reduce the risk of relapse after TFR attempts
- Response to asciminib in patients with pre-existing BCR::ABL1 mutations other than T315I, or treatment approaches in patients with emerging mutations under asciminib, including compound mutations

CML- BC and Ph+ ALL

- Efficacy and safety of Asciminib in selected ALL settings (PH+, Ph-Like)
- Exploratory high-risk advanced phase CML populations such as patients with additional genomic alterations
- TKI- based combinations addressing high unmet need populations (CML-AP/BC)

Out of scope

- Use of Non BCR-ABL diseases

Iptacopan (Fabhalta)

With Drug

- Mechanistic studies in PNH
- Studies evaluating complement factors associated with or predictive of treatment outcome in PNH
- Studies evaluating effectiveness, safety and management of Iptacopan in PNH patients treated in the real-world setting
- Studies evaluating PNH treated patients in the context of bone marrow disorders, such as AA, in the real-world setting
- Studies evaluating the role of factor B inhibition in hematologic complement mediated diseases

Without drug

- Complement mediated diseases in Hematology
- Role of complement system in disease evolution
- Approaches to facilitating and expediting diagnosis
- Identification of biomarkers that leads to better characterization, management or correlation with outcomes
- Burden of disease (clinical, economic, and/or humanistic burden)

- Epidemiology studies (incl. registries)

Out of scope

- Pediatric studies
- Clinical trials exploring different dosing regimens as currently investigated
- Clinical trials combining Iptacopan with immunosuppressant and anti-C5 treatments
- Head-to-head comparisons
- Studies in other non complement mediated hematologic diseases

Ribociclib (Kisqali)

HR+/HER2- Studies in Breast Cancer

- Exploring ribociclib with novel/emergent compounds
- Utilizing real-world data (RWD) and/or digital health technologies
- Enhances the treatment experience of patients

Out of scope

- Any area outside HR+/HER2- breast cancer
- Any study in overlap with ongoing Novartis – sponsored/supported studies

[177Lu]Lu-PSMA-617 (Pluvicto)

- Investigating retreatment or extended treatment with ^{177}Lu-PSMA-617
- Real-world evidence in prostate cancer for ^{177}Lu-PSMA-617
- Health disparities in advanced prostate cancer

177Lu DOTATATE (Lutathera) / 68Ga DOTATATE (Netspot)

GEP & Bronchopulmonary NET

- Re-treatment/Re-challenge with Lutathera (after initial 4 cycles)
- Combinations with other agents with potential to improve efficacy
- Sequencing studies
- Long-term safety
- Efficacy/Safety of Lutathera in specific patient subgroups

Other SSTR+ Tumors

- Role of Lutathera in the management of patients with other SSTR-positive tumors

NETSPOT for Imaging

- Role of Netspot in GEP-NET and other SSTR2+ tumors

FAP [177Lu] Lu-FAP-2286

Imaging Studies in FAP-expressing solid tumors

- Role of FAP PET in diagnosis, staging, clinical decision-making, and treatment response
- Studies exploring FAP PET as an imaging biomarker: Correlation with other biomarkers such as histological/molecular/genetic subtype
- Understanding FAP expression in benign/inflammatory processes in relation to FAP RLT safety and patient selection for therapy

Therapeutic Studies

- Role of 177Lu-FAP RLT in FAP-expressing solid tumors

- Use of 177Lu-FAP RLT in combination with standard of care therapies and/or immuno-oncology agents
- Studies investigating the effect of 177Lu-FAP RLT in cancer-associated fibroblasts and tumor microenvironment
- Evaluation of optimal dosing regimens in subpopulations and combinations
- Correlation of RLT efficacy with predictive biomarkers and FAP PET uptake
- Studies exploring alternate routes of administration to improve safety and efficacy

^{225}Ac-PSMA-617 / ^{225}Ac-PSMA-R2

- Investigating alternative dosing regimens (cycles, frequency) with ^{225}Ac-PSMA-617 in mCRPC
- Radioligand therapy in neoadjuvant setting for localized prostate cancer
- Use of ^{225}Ac-PSMA-617 in adjuvant setting in combination with EBRT + ADT +/- abiraterone in patients with localized prostate cancer post prostatectomy with N1M0 on PSMA PET
- Use of ^{225}Ac-PSMA-617 post definitive therapy for localized prostate cancer with biochemical recurrence and PSMA-PET M0 disease
- Use of PSMA-targeted PET imaging agents in prostate cancer (e.g., patient selection, treatment assessment)
- Use of ^{225}Ac-PSMA-617 in combination with other agents in mHSPC or mCRPC
- Treatments up-regulating PSMA expression in prostate cancer
- Use of >6 cycles of ^{225}Ac-PSMA-617 in patients with mHSPC or mCRPC
- Use of ^{225}Ac-PSMA-617 in prostate cancer patients with distinct mutations (e.g., PTEN-loss, AKT, DDR)
- Use of ^{225}Ac-PSMA-617 in patients with low or no PSMA expression in mCRPC
- Real-world evidence in prostate cancer for ^{225}Ac-PSMA-617
- Health disparities in advanced prostate cancer
- Sequencing with 177Lu-PSMA-617

CRM
Pelacarsen

Non-drug IITs

Epidemiology associated with elevated Lp(a)

- Patient characterization, identification, and genetic risk across sub-groups
- Association & impact on different types of CVD (ischemic stroke, PAD), polyvascular disease, and other CV-related diseases

Distinct and unique pathophysiology of Lp(a) related to CVD

- Insights on the pro-thrombotic mechanisms impacted by Lp(a)
- Unique features of Lp(a)

Patient perception on contribution of Lp(a) to CVD and CV risk

Lp(a) testing and global CV risk management

- Implementation of Lp(a) testing in CVD risk evaluation
- Clinical and economic value of Lp(a) testing

Out of scope

- Comparison / association with LDL-C
- Non-cardiovascular related diseases

Inclisiran (Leqvio)

- ASCVD MOA – atherosclerotic plaque composition/changes
- Differentiation of inclisiran vs other LLTs in Real World setting – e.g., adherence, implementation

Atrasentan for IgAN Indication (Vanrafia)

Disease-related: including but not limited to IgAN, FSGS, Alport Syndrome, post-kidney transplant

- Studies evaluating the role of the endothelin pathway in proteinuric kidney diseases (e.g. IgAN, FSGS, Alport Syndrome, post-kidney transplant).
- Innovative diagnostic approaches beyond biopsy and prognostic approaches for IgAN and FSGS.
- Approaches to improve profiling (biomarkers, genetics, imaging, histopathology) of patients with IgAN and FSGS.
- Epidemiological studies and burden of disease (clinical, economic and/or humanistic burden) in patients with proteinuric kidney diseases.
- Patient journey mapping and practice change initiatives to improve outcomes and reduce disparities.

Drug-related

- Studies evaluating pre-clinical, mechanistic and clinical effects of atrasentan in patients with proteinuric kidney diseases (included, but not limited to IgAN, and post-kidney transplant), including biomarker analyses, specific patient subgroups, and broader physiological impacts (e.g. inflammation, fibrosis, and pain).
- Studies on combination strategies with atrasentan in IgAN.

Out of scope

- Pediatric studies (with drug).
- Studies exploring different dosing regimens than currently FDA-approved dose.
- Head-to-head comparisons with other approved products.
- Studies including patients with eGFR <15 ml/min/1.73m^2 (CKD stage 5).

Iptacopan

Disease-related: including but not limited to IgAN, C3G, IC-MPGN, aHUS, LN, AAV, FSGS, post-kidney transplant, IgAV with nephrits

- Studies evaluating the role of the complement system in complement-mediated kidney diseases.
- Innovative diagnostic approaches beyond biopsy and prognostic approaches for complement-mediated kidney diseases.
- Approaches to improve profiling (i.e. biomarkers, genetics, imaging, histopathology) of patients with complement-mediated kidney diseases.
- Epidemiological studies and burden of disease (clinical, economic and/or humanistic burden) in patients with complement-mediated kidney diseases.
- Patient journey mapping and practice change initiatives to improve outcomes and reduce disparities.

Drug-related

- Studies evaluating pre-clinical, mechanistic, and clinical effects of iptacopan in patients with complement-mediated kidney diseases (e.g. IgAN, C3G, IC-MPGN, aHUS, post-kidney transplant, IgAV with nephritis) including biomarker analyses, and specific patient subgroups (e.g. high crescent, RPGN, corticosteroid-resistant).
- Studies on combination strategies with iptacopan in IgAN.

Out of scope

- Pediatric studies (with drug).
- Head-to-head comparisons with other approved products.
- Studies including patients with GFR <20 ml/min/1.73m^2.

Neuroscience

Ofatumumab (Kesimpta)

Multiple Sclerosis

- The experience of use of OMB in sub-populations of RMS (e.g., AA and Hispanic patients, and age)

- The impact of OMB on MS comorbidities and patient-centric outcomes
- The therapeutic role of OMB in MS: Efficacy, safety, tolerability, use in treatment naive patients
- The impact of OMB on both fluid and digital biomarkers in MS
- The MS pathophysiology (including MoA of OMB and its effects on MS pathophysiology) and burden of disease of MS (including impact of OMB)
- The innovative neuroimaging techniques used to measure biomarkers of MS disease/MS inflammation/axonal integrity and function (including effects of OMB)
- The long-term impact on the immune system and long-term safety with B-cell therapies
- Different B-cell depleting therapies have a differential impact on the functioning of the immune system over time, especially on the non-B-cell compartment

Remibrutinib

Multiple Sclerosis

- The impact on CNS – BBB transmigration, microglial impact (activation)
- The impact on biology of progression – PET imaging impact, cognition, fatigue, depression outcomes
- The impact on imaging – SELs, PRLs, cortical lesions impact
- The role for remibrutinib in sequencing of treatments
- The proteome profiling effects of remibrutinib

Myasthenia Gravis

- Impact of remibrutinib on gMG
- Development of biomarkers and endpoint exploration for clinical trial use

Zolgensma IV

In Scope

- Demonstrating or validating care needs for SMA populations post Zolgensma IV Treatment-safety related items
- Value of Zolgensma IV : Cost of care, Quality of life, and Caregiver Burden-Cost effectiveness
- Methods/Processes to assess the efficacy and durability of Zolgensma IV (e.g. bulbar function)
- Biomarkers for efficacy

Out of Scope

- Clinical Trials involving Zolgensma IV re-dosing
- Study of Zolgensma IV alternative doses/maximum dose
- Basic Science research that request use of Zolgensma IV

OAV101 IT

In Scope

- Interventional Studies of OAV101 IT in patients not included in clinical trials (e.g. independently ambulant SMA patients, patients >18 years, severe scoliosis) and patients with AAV9 titers >1:50
- Non-interventional Studies of OAV101 IT assessing sleep, bulbar function, scoliosis and respiratory function, head steadiness and independence.
- Studies on biomarkers assessing clinical response to OAV101 IT

Out of Scope

- Clinical Trials involving OAV101 IT re-dosing or OAV IT dosing following OAV IV
- Study of OAV101 IT alternative doses/maximum dose
- Head-to-head comparison with other therapies and combination with other MDT
- Studies of OAV101 IT in patients under 2 years of age.
- Comparative studies between Zolgensma IV and OAV101 IT

Ianalumab

- Sjogren's disease US epidemiology
- Sjogren's disease classification and clinical assessment
- Sjogren's disease progression: use of ultrasounds, clinical assessments and or biomarkers
- Sjogren's symptoms: evidence generation with existing PROs or new SjD symptom modalities
- Sjogren's disease organ domains: generation of evidence in key disease domains
- Sjogren's disease and concomitant conditions (i.e., rheumatoid arthritis, lupus, etc.) and outcomes
- Sjogren's disease in subpopulations (AA, Hispanic, etc.) and outcomes
- Sjogren's disease burden: clinical, social, economical, and humanistic aspects

Remibrutnib -Urticaria

Disease Related Research

- Population-based epidemiology studies; studies investigating the impact of urticaria on patients; studies of real-world treatment patterns (incl. e.g. overuse of corticosteroids, impact on sleep); studies of patient preference, patient experience and satisfaction (qualitative).
- Studies employing digital technology e.g. *in silico* models, AI-enabled/machine learning techniques, telemedicine etc. to predict disease trajectories, treatment response, disease modification, etc.
- Studies investigating innovative tools to support urticaria management, e.g. digital applications, sleep related.
- Long-term CSU/CindU observational studies and secondary use of data.

Clinical Studies

- Studies with Remibrutinib in CSU/CindU,
- Poof of concepts in new allergic and dermatologic indications.

Mechanistic Studies

- Mechanistic studies assessing the effects of Remibrutinib on mast cells, basophils, B-cells and other relevant immune pathways *in vitro* or *ex vivo.*

Optional Out of Scope

- Head-to-head comparisons of Remibrutinib with other active treatments.
- Studies investigating Remibrutinib in combination with biologics.
- Alternative dosing regimens to 25 mg b.i.d developed in the CSU phase 3 clinical program.
