ForPatients
by Roche

Advanced or Metastatic Esophageal Squamous Cell Carcinoma

A Study of RO7121661 and RO7247669 Compared With Nivolumab in Participants With Advanced or Metastatic Squamous Cell Carcinoma of the Esophagus

Trial Status	Trial Runs In	Trial Identifier
Completed	18 Countries	NCT04785820 2020-004606-60 BP42772

The information is taken directly from public registry websites such as ClinicalTrials.gov, EuClinicalTrials.eu, ISRCTN.com, etc., and has not been edited.

Official Title:

A 3-Arm, Randomized, Blinded, Active-Controlled, Phase II Study of RO7121661, a PD1-TIM3 Bispecific Antibody and RO7247669, a PD1-LAG3 Bispecific Antibody, Compared With Nivolumab in Participants With Advanced or Metastatic Squamous Cell Carcinoma of the Esophagus

Trial Summary:

This is a Phase II, randomized, blinded, active-controlled, global, multicenter study designed to evaluate the safety and efficacy of lomvastomig and tobemstomig, compared with nivolumab, in patients with advanced or metastatic esophageal squamous-cell carcinoma (ESCC) refractory or intolerant to fluoropyrimidine- or taxane- and platinum-based regimen. Following approval of the protocol amendment version 3, recruitment into the lomvastomig arm has been stopped. The decision to stop recruitment for lomvastomig was based on strategic considerations and not based on emerging safety and/or efficacy data. The benefit/risk assessment for lomvastomig remains unchanged. The study was planned to enroll participants randomized in a 1:1:1 ratio to receive lomvastomig, tobemstomig, or nivolumab. With version 3 of the protocol, recruitment into the lomvastomig arm has stopped, and moving forward, participants will be randomized in a 1:1 ratio to receive either tobemstomig or nivolumab.

Hoffmann-La Roche	**Phase 2**
Sponsor	Phase

NCT04785820 2020-004606-60 BP42772
Trial Identifiers

Eligibility Criteria:

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Gender	Age	Healthy Volunteers
All	#18 Years	No

Inclusion Criteria:

- Advanced or metastatic, histologically confirmed esophageal squamous-cell carcinoma (ESCC)
- Patients who have previously received 1 line of treatment with either a fluoropyrimidine- and platinum- or a taxane- and platinum-based regimen in non-curative intention prior to randomization; or patients who received treatment with a fluoropyrimidine-/taxane- and platinum-based regimen in curative intention and had recurrence or progression within 24 weeks after the last dose of the treatment
- Radiologically measurable disease according to RECIST v1.1. Previously irradiated lesions should not be counted as target lesions unless clearly progressed after the radiotherapy
- Eastern Cooperative Oncology Group (ECOG) Performance Status 0-1
- A life expectancy of at least (#)12 weeks
- Tissue samples must be provided for analysis of anti-programmed death ligand-1 (PD-L1) tumor positivity
- Adverse events from any prior radiotherapy, chemotherapy, or surgical procedure must have resolved to Grade #1, except alopecia (any grade), vitiligo, endocrinopathy managed with replacement therapy, and Grade 2 peripheral neuropathy
- Adequate cardiovascular, hematological, liver, and renal function
- Serum albumin #25 grams per liter (g/L),
- For participants not receiving therapeutic anticoagulation: prothrombin time (PT) and activated partial thromboplastin time #1.5 times (×) the upper limit of normal (ULN); for participants receiving therapeutic anticoagulation: stable anticoagulant regimen
- A female participant is eligible to participate if she is not pregnant, not breastfeeding, not a woman of childbearing potential (WOCBP), or a WOCBP who agrees to remain abstinent (refrain from heterosexual intercourse) or use contraceptive methods during the treatment period and for at least 5 months after the final dose of study drug and have a negative pregnancy test (blood) within the 7 days prior to randomization.
- A male participant must remain abstinent (refrain from heterosexual intercourse) or use contraceptive measures such as a condom plus an additional contraceptive method and refrain from donating sperm during the treatment period and for at least 5 months after the final dose of study drug

Exclusion Criteria:

- Pregnancy, lactation, or breastfeeding
- Known hypersensitivity to any of the components of RO7121661, RO7247669, or nivolumab, including but not limited to, hypersensitivity to Chinese hamster ovary cell products or other recombinant human or humanized antibodies
- Patients with significant malnutrition. Patients whose nutrition has been well controlled for #28 days prior to randomization may be enrolled
- Evidence of complete esophageal obstruction not amenable to treatment
- Higher risk of bleeding or fistula caused by esophageal lesions invading adjacent organs (aorta or tracheobronchial tree). Patients with manageable fistula may be included at the Investigator's discretion.
- Symptomatic central nervous system (CNS) metastases
- Spinal cord compression not definitively treated with surgery and/or radiation or without evidence that disease has been clinically stable for #14 days prior to randomization
- Active or history of carcinomatous meningitis/leptomeningeal disease

- Asymptomatic CNS primary tumors or metastases if they have requirement for steroids or enzyme inducing anticonvulsants in the last 28 days prior to randomization
- Uncontrolled tumor-related pain. Participants requiring pain medication must be on a stable regimen at study entry
- Active second malignancy (with some exceptions)
- Evidence of significant, uncontrolled concomitant diseases that could affect compliance with the protocol or interpretation of results, including diabetes mellitus, history of relevant pulmonary disorders, known autoimmune diseases or immune deficiency, or other diseases with ongoing fibrosis (such as scleroderma, pulmonary fibrosis, emphysema, neurofibromatosis, palmar/plantar fibromatosis, etc.).
- Encephalitis, meningitis, or uncontrolled seizures in the year prior to informed consent
- Significant cardiovascular/cerebrovascular disease within 6 months prior to randomization
- Known active or uncontrolled bacterial, viral, fungal, mycobacterial (including but not limited to tuberculosis [TB] and typical mycobacterial disease), parasitic, or other infection (excluding fungal infections of nail beds) or any major episode of infection requiring treatment with intravenous (IV) antibiotics or hospitalization (relating to the completion of the course of antibiotics, except if for tumor fever) within 28 days prior to randomization
- Known clinically significant liver disease, including alcoholic hepatitis, cirrhosis, and inherited liver disease.
- Major surgical procedure or significant traumatic injury (excluding biopsies) within 28 days prior to randomization, or anticipation of the need for major surgery during the course of the study
- Any other diseases, metabolic dysfunction, physical examination finding, or clinical laboratory finding giving reasonable suspicion of a disease or condition that contraindicates the use of an investigational drug or that may affect the interpretation of the results or render the participant at high risk from treatment complications
- Dementia or altered mental status that would prohibit informed consent
- Uncontrolled pleural effusion, pericardial effusion, or ascites requiring recurrent drainage procedures (expected to occur once monthly or more frequently)
- Active or history of autoimmune disease or immune deficiency
- Positive human immunodeficiency virus (HIV) test at screening
- Positive hepatitis B surface antigen (HBsAg) or positive total hepatitis B core antibody (HBcAb) test at screening
- Positive hepatitis C virus (HCV) antibody test at screening
- Prior cancer therapy with any immunomodulatory agents including checkpoint inhibitors (CPIs; such as anti-PDL1/PD1, anti-CTLA-4, anti-LAG3, anti-TIM3)
- Vaccination with live vaccines within 28 days prior to randomization, or anticipation that a live attenuated vaccine will be required during the study
- Treatment with therapeutic oral or IV antibiotics within 14 days prior to randomization
- Concurrent therapy with any other investigational drug (defined as treatment for which there is currently no regulatory authority approved indication) 28 days or 5 half-lives of the drug (whichever is shorter) prior to randomization
- Treatment with immune-modulating and immune suppressive agents/medication 5 half-lives or 28 days (whichever is shorter) prior to randomization
- Regular immunosuppressive therapy (i.e., for organ transplantation, chronic rheumatologic disease)
- Radiotherapy within the last 28 days before start of study drug treatment is not allowed, with the exception of limited palliative radiotherapy
- Prior treatment with adoptive cell therapies, such as chimeric antigen receptor T cells (CAR-T) therapies