CLINICAL TRIAL FACT SHEET

Clinicaltrials.gov Identifier: NCT03319667

A phase III, randomized, open-label, multicenter study assessing the clinical benefit of isatuximab in combination with bortezomib (Velcade®), lenalidomide (Revlimid®), and dexamethasone versus bortezomib, lenalidomide, and dexamethasone in patients with newly diagnosed multiple myeloma not eligible for transplant

(IMROZ study)

Trial Description:

Approximately 440 patients with newly diagnosed myeloma who are not eligible for stem cell transplant will be randomly assigned by a computer to one of two treatment groups called study "arms." Patients will know to which of the arms they have been assigned. Patients in the experimental arm will receive a combination of anti-CD38 monoclonal antibody isatuximab (formerly known as SAR650984), bortezomib (brand name Velcade), lenalidomide (brand name Revlimid), and dexamethasone (IsaVRd), followed by continuous therapy with isatuximab, lenalidomide, and dexamethasone (IsaRd). Patients in the comparator arm of the study will receive a combination of bortezomib, lenalidomide, and dexamethasone (VRd) followed by continuous treatment with lenalidomide and dexamethasone (Rd). Patients randomized to receive Rd maintenance whose disease progresses during maintenance therapy may cross over to receive the isatuximab, lenalidomide, and dexamethasone combination.

Trial Objectives:

The primary objective of this trial is to determine the possible benefit of isatuximab in combination with bortezomib, lenalidomide, and dexamethasone (IsaVRd) in prolonging progression-free survival (remission duration) as compared with bortezomib, lenalidomide, and dexamethasone (VRd) in patients with newly diagnosed myeloma. Other objectives include evaluating the following in both study arms:

- The very good partial response (VGPR) rate (at least a 90% drop in the amount of monoclonal protein).
- The complete response (CR) rate (no remaining monoclonal protein detectable).
- The minimal residual disease-negative (MRD-negative) rate in patients with CR or VGPR.
- Time to disease progression.
- Progression-free survival (PFS) in MRD-negative patients.
- Duration of response.
- PFS following the next line of therapy after the clinical trial (PFS2).
- Overall survival (OS).
- Overall response rate (ORR).
- Safety.
- Disease-specific and general quality of life.

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INTERNATIONAL MYELOMA FOUNDATION

International Myeloma Foundation
12650 Riverside Drive, Suite 206, North Hollywood, CA 91607 USA
Telephone: 800.452.CURE (2873) (USA & Canada) 818.487.7455 (worldwide) • TheIMF@myeloma.org • myeloma.org

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(continued)

Trial Design:

Experimental Arm – Induction treatment (IsaVRd)

- Patients will receive four 6-week cycles of isatuximab given intravenously (IV, or into a vein) on days 1, 8, 15, 22, and 29 in cycle 1, and on days 1, 15, and 29 in all subsequent cycles.
- Patients will receive bortezomib subcutaneously (SC, or as an injection) on days 1, 4, 8, 11, 22, 25, 29, and 32 of each 6-week cycle.
- Patients will receive oral lenalidomide on days 1–14 and 22–35 of each 6-week cycle.
- Patients will receive oral or IV dexamethasone on days 1, 2, 4, 5, 8, 9, 11, 12, 15, 22, 23, 25, 26, 29, 30, 32, and 33 of each 6-week (42-day) cycle.

Experimental Arm – Continuous treatment (IsaRd)

- Patients will receive 4-week cycles of IV isatuximab on days 1 and 15 of each cycle.
- Patients will receive oral lenalidomide on days 1–21 of each 4-week cycle.
- Patients will receive oral or IV dexamethasone on days 1, 8, 15, and 22 of each 4-week cycle.

Comparator Arm – Induction treatment

- Patients will receive four 6-week cycles of SC bortezomib on days 1, 4, 8, 11, 22, 25, 29, and 32.
- Patients will receive oral lenalidomide on days 1–14 and 22–35 of each 6-week cycle.
- Patients will receive oral or IV dexamethasone on days 1, 2, 4, 5, 8, 9, 11, 12, 15, 22, 23, 25, 26, 29, 30, 32, and 33 of each 6-week (42-day) cycle.

Comparator Arm – Continuous treatment

- Patients will receive oral lenalidomide on days 1–21 of each 4-week cycle.
- Patients will receive oral or IV dexamethasone on days 1, 8, 15, and 22 of each 4-week cycle.

Comparator Arm – Crossover

- Patients who exhibit disease progression while on maintenance therapy with Rd may cross over to receive isatuximab, lenalidomide, and dexamethasone.

Duration of Treatment:

The duration of the study for each patient will include a screening period of up to 4 weeks, an induction period of 24 weeks, a continuous treatment period, and a crossover period (when applicable). The cycle duration is 28 ± four days during the continuous treatment and crossover periods.

Other Medications:

Participants receiving isatuximab will be given oral acetaminophen (Tylenol®, paracetamol, or equivalent), intravenous ranitidine (Zantac®), and intravenous diphenhydramine (Benadryl® or equivalent) before each dose of isatuximab.

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(IMROZ study)

(continued)

Inclusion Criteria:

- Symptomatic multiple myeloma (according to International Myeloma Working Group criteria).
- Newly diagnosed myeloma not eligible for transplant due to age (≥ 65 years), or patients < 65 years with other medical conditions preventing the possibility of transplant, or patient's refusal of transplant.
- Evidence of measurable disease.
- Written informed consent.

Exclusion Criteria:

- Prior treatment for multiple myeloma.
- Asymptomatic multiple myeloma.
- Any other prior or ongoing disease/health conditions incompatible with the study objectives.
- Organ function values not met.
- Poor overall health status.
- Hypersensitivity to the study medications.
- Female patients who are pregnant, breastfeeding, or of childbearing potential and unwilling to use recommended contraception methods.
- Male patients who refuse to use recommended contraception methods.

Locations Enrolling Patients and Contact Information:

For site information, send an email including one or more of the below site numbers to Contact-Us@sanofi.com

Australia
Investigational Site Number 0360008
Nedlands, Australia, 6009

Investigational Site Number 0360002
Wollongong, Australia, 2500

Czechia
Investigational Site Number 2030002
Brno, Czechia, 62500

Investigational Site Number 2030003
Ostrava – Poruba, Czechia, 70852

Investigational Site Number 2030001
Praha 2, Czechia, 12808

France
Investigational Site Number 2500001
Nantes Cedex 01, France, 44093

Investigational Site Number 2500006
Paris Cedex 12, France, 75571

Japan
Investigational Site Number 3920005
Morioka-Shi, Japan

Investigational Site Number 3920004
Shibuya-Ku, Japan

Investigational Site Number 3920003
Sunto-Gun, Japan

Investigational Site Number 3920001
Suwa-Shi, Japan

Investigational Site Number 3920002
Yamagata-Shi, Japan

Korea, Republic of
Investigational Site Number 4100001
Seoul, Korea, 03080

Investigational Site Number 4100002
Seoul, Korea, 06351

New Zealand
Investigational Site Number 5540002
Wellington, New Zealand

Turkey
Investigational Site Number 7920001
Ankara, Turkey, 06500

Investigational Site Number 7920002
İstanbul, Turkey

United States
Investigational Site Number 8400003
Billings, Montana

Investigational Site Number 8400008
Chattanooga, Tennessee

Investigational Site Number 8400001
Houston, Texas

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