P-066

# Prophylactic Interventions for Oral Toxicities With the GPRC5D×CD3 Bispecific Antibody Talquetamab in Relapsed/Refractory Multiple Myeloma: An Open-Label, Phase 2, Randomized Study (TALISMAN)

Rakesh Popat[1], Alexa Laheij[2], Niels WCJ van de Donk[3], Richard L Doty[4], Jim Omel[5], Brea Lipe[6], Leo Rasche[7], Ajai Chari[8], Kelly Kato[9], Ken Tian[10], Deeksha Vishwamitra[10], Jacqueline Speier[10], Mathilde Durand[11], Margaret Northup[12], Ibrahim Saber[13], William Prada[13], Kathleen Gray[14], Gloria Aguilar[15], Larysa Sanchez[16]

[1]University College London Hospitals NHS Foundation Trust, London, UK; [2]University of Amsterdam and Vrije Universiteit, Amsterdam, the Netherlands, and Amsterdam University Medical Centers, University of Amsterdam, Amsterdam, the Netherlands; [3]Amsterdam University Medical Center, Vrije Universiteit Amsterdam, Amsterdam, the Netherlands; [4]University of Pennsylvania Smell and Taste Center, Philadelphia, PA, USA; [5]The Central Nebraska Myeloma Support Group, Grand Island, NE, USA; [6]University of Rochester Medical Center, Rochester, NY, USA; [7]University Hospital of Würzburg, Würzburg, Germany; [8]University of California, San Francisco, San Francisco, CA, USA; [9]Janssen Global Services, Raritan, NJ, USA; [10]Janssen Research & Development, Spring House, PA, USA; [11]Janssen Global Services, Basel, Switzerland; [12]Janssen Research & Development, Titusville, NJ, USA; [13]Janssen Research & Development, Raritan, NJ, USA; [14]Janssen Research & Development, Bridgewater, NJ, USA; [15]Janssen Biologics B.V. Leiden, the Netherlands; [16]Icahn School of Medicine at Mount Sinai, New York, NY, USA

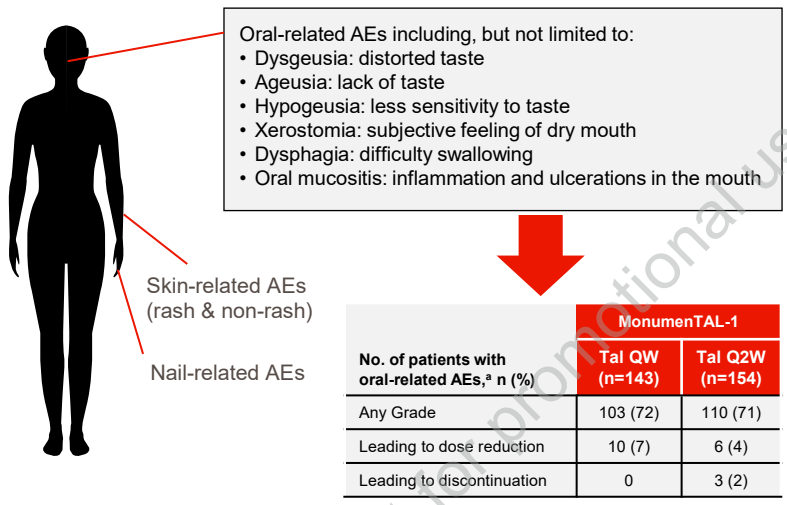
## Introduction

- G protein–coupled receptor family C group 5 member D (GPRC5D), a novel antigen, has limited expression in normal tissue but is highly expressed on malignant plasma cells, making it a validated target in multiple myeloma[1-4]
- Talquetamab is the first approved GPRC5D-targeting bispecific antibody for the treatment of patients with triple-class exposed relapsed/refractory multiple myeloma (RRMM) based on results from the MonumenTAL-1 study (NCT03399799/ NCT04634552)[1,5-7]
- On-target, off-tumor adverse events (AEs), including nail, skin (rash and non-rash), and oral toxicities, have been reported with GPRC5D-targeted therapies, including talquetamab[7,8] (**Figure 1**)
- Although talquetamab demonstrated high overall response rates (ORRs) of ≥70% and durable responses in the MonumenTAL-1 study, early onset oral toxicities, including dysgeusia, can impact patients' treatment experience[7]
- Current methods used to assess oral toxicities in clinical trials are not standardized and may not capture the impact on patients' experience[8]; thus, more formal, validated approaches are warranted

### Objective

- This study aims to better understand oral toxicities, and investigate prophylactic interventions to prevent and/or limit the severity of talquetamab-related oral toxicities

**Figure 1: AEs associated with GPRC5D-targeting therapies, including talquetamab**




| No. of patients with oral-related AEs,[a] n (%) | MonumenTAL-1 Tal QW (n=143) | MonumenTAL-1 Tal Q2W (n=154) |
|---|---|---|
| Any Grade | 103 (72) | 110 (71) |
| Leading to dose reduction | 10 (7) | 6 (4) |
| Leading to discontinuation | 0 | 3 (2) |

[a]Including ageusia, dysgeusia, hypogeusia, and taste disorder.
Q2W, every other week; QW, weekly; tal, talquetamab.

## Methods

### Study design and patients

- TALISMAN is a randomized, multicenter, open-label, phase 2 study (**Figure 2**)
- Patients are at least 18 years of age with documented RRMM per International Myeloma Working Group criteria and have measurable and progressive disease at screening
- At screening, patients must have an Eastern Cooperative Oncology Group performance status (ECOG PS) of 0 or 1 and cannot have a severe score for dysgeusia per the Waterless Empirical Taste Test (WETT) scale
- Patients must be triple-class exposed, including to a proteasome inhibitor, immunomodulatory drug, and an anti-CD38 monoclonal antibody and be considered for treatment with talquetamab
- Patients who have received prior GPRC5D-targeted therapy are excluded from the study
- Target enrollment is 120 patients across study sites in 6 countries (**Figure 3**)

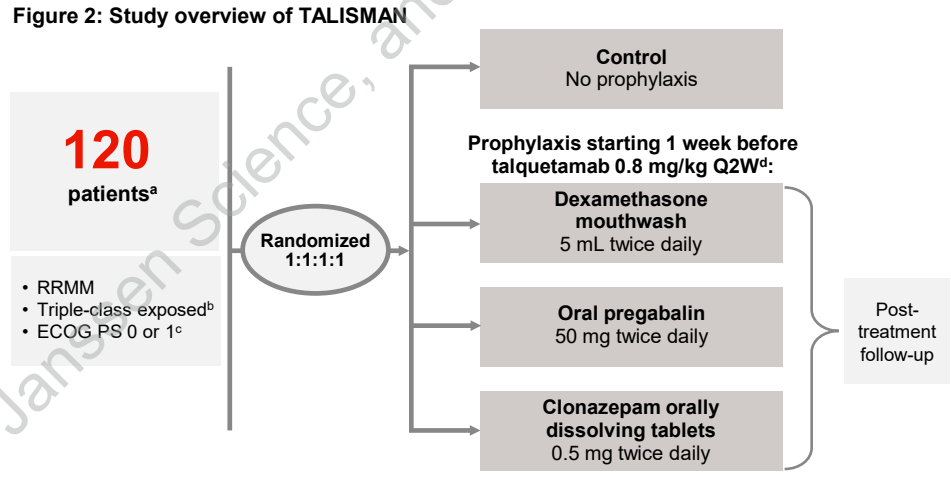
### Treatment and procedures

- Patients are equally randomized to 1 of 4 cohorts: 1 control cohort and 3 experimental cohorts each receiving the following prophylaxis: dexamethasone mouthwash, oral pregabalin, or clonazepam orally dissolving tablets (**Figure 2**)
  - The study will be conducted in 3 phases: screening (up to 28 days), treatment, and follow-up
  - An interim data review will be conducted to evaluate study cohorts after approximately 15 patients have been treated with talquetamab for at least 3 cycles to avoid prolonged prophylaxis with no positive effects
- Patients will receive their prophylaxis 1 week before starting talquetamab, which will be administered at 0.8 mg/kg Q2W after 3 step-up doses
  - A dose frequency reduction to every 4 weeks is permitted if the patient achieves a very good partial response (VGPR) or better or partial response (PR) or better starting at cycle 5 or 7, respectively
  - Patients will receive talquetamab until progressive disease, death, intolerable toxicity, withdrawal of consent, discontinuation, or end of study, whichever occurs first
- Oral toxicities are evaluated with the following key procedures: taste assessment using WETT strips, patient-reported outcomes (PROs), optional tongue and/or salivary gland biopsies (only at selected sites), microbiome analysis via tongue swab (control cohort only), and salivary flow and specific protein content assessments
- Smell is evaluated by a smell assessment using the University of Pennsylvania Smell Identification Test and threshold testing

### Assessment and endpoints

- Endpoints are summarized in the **Table**
- AEs will be graded by Common Terminology Criteria for Adverse Events (CTCAE) v5.0
- Cytokine release syndrome and immune effector cell–associated neurotoxicity syndrome will be graded by American Society for Transplantation and Cellular Therapy criteria
- Qualitative patient interviews will be conducted in the US to better understand patient experience

**Figure 2: Study overview of TALISMAN**




[a]Target enrollment. [b]Including a proteasome inhibitor, immunomodulatory drug, and an anti-CD38 monoclonal antibody. [c]ECOG PS of 2 or 3 permitted once physical limitations are stable. [d]With 3 step-up doses.

**Figure 3: Countries with open or planned study sites for TALISMAN**


**Table: Study endpoints**

**Primary endpoint**

- The overall incidence, severity, onset, and rate of resolution/improvement of dysgeusia at 3 and 6 months determined by the total WETT score

**Secondary endpoints**

**Efficacy of prophylaxis**
- Change from baseline in WETT score over time
- Percentage of time with dysgeusia
- Change from baseline in body weight and BMI over time
- Change from baseline in the results of the smell identification and smell detection threshold test

**Efficacy of talquetamab**
- ORR (≥PR), rate of ≥VGPR, rate of ≥CR, duration of response, time to response

**Safety**
- Incidence, severity, timing, and duration of AEs, including oral toxicities (dysgeusia, oral mucositis, dysphagia, and xerostomia)

**PROs**
- Change from baseline in health-related quality-of-life assessments, including EORTC QLQ-C30 and EORTC QLQ-OH15
- Proportion of patients who report oral symptoms using the PRO-CTCAE, Short Xerostomia Inventory, Epstein Taste Scale, and Scale of Subjective Total Taste Acuity

BMI, body mass index; CR, complete response; EORTC QLQ-C30, European Organisation for Research and Treatment of Cancer quality of life questionnaire core-30 item; EORTC-QLQ-OH15, European Organisation for Research and Treatment of Cancer quality of life questionnaire-Oral Health.

## Current status

TALISMAN opened for enrollment in August 2024

## Registration

TALISMAN is a randomized, multicenter, open-label, phase 2 study

ClinicalTrials.gov, NCT06500884

This study will provide potential strategies to manage, prevent, and decrease the severity of talquetamab-related oral toxicities; needed data on taste-related assessment tools; and assessments of the potential impact of toxicities on patient treatment experience

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Poster

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Multiple Myeloma

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