Summary Table of Study Protocol

Title	Assessment of the 'Managing Advanced Cancer Pain Together' (MACPT) tool to facilitate communication on total cancer pain between advanced cancer patients and their healthcare professionals
Protocol version identifier	20160376
Date of last version of the protocol	18 January 2018
EU Post Authorisation Study (PAS) Register No	NA
Active Substance	NA
Medicinal Product	NA
Product Reference	NA
Procedure Number	NA
Marketing Authorisation Holder(s)	Amgen Inc.
Joint PASS	No
Research Question and Objectives	The research focus is the assessment of a paper-based conversation tool, the 'Managing Advanced Cancer Pain Together' (MACPT) conversation tool, developed to support a comprehensive pain dialogue between the patient and healthcare practitioner (HCP) during their routine face-to-face consultation. The primary objective is to assess the impact of the MACPT tool on patient- and HCP- reported overall satisfaction of their conversation during routine standard of care (SoC) consultations. The secondary objectives are to assess the impact of the MACPT tool on patient- and HCP- reported satisfaction on specific aspects of their conversation during face-to-face routine SoC consultations, to describe the frequency of the tool words selected by the patients, and to describe both patient- and HCP-reported usefulness of the MACPT conversation tool to identify key aspects of the patient's total pain experience. Other planned objectives will explore the perceptions around patient-HCP communication across each side of the conversations.
Country(-ies) of Study	UK, France and Germany

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Investigator's Agreement

I have read the attached protocol entitled "Assessment of the 'Managing Advanced Cancer Pain Together' (MACPT) tool to facilitate communication on total cancer pain between advanced cancer patients and their healthcare professionals" dated 18 January 2018, and agree to abide by all provisions set forth therein.

I agree to ensure that the confidential information contained in this document will not be used for any purpose other than the evaluation or conduct of the clinical investigation without the prior written consent of Amgen Inc.

Signature

PPD

Date (DD Month YYYY)

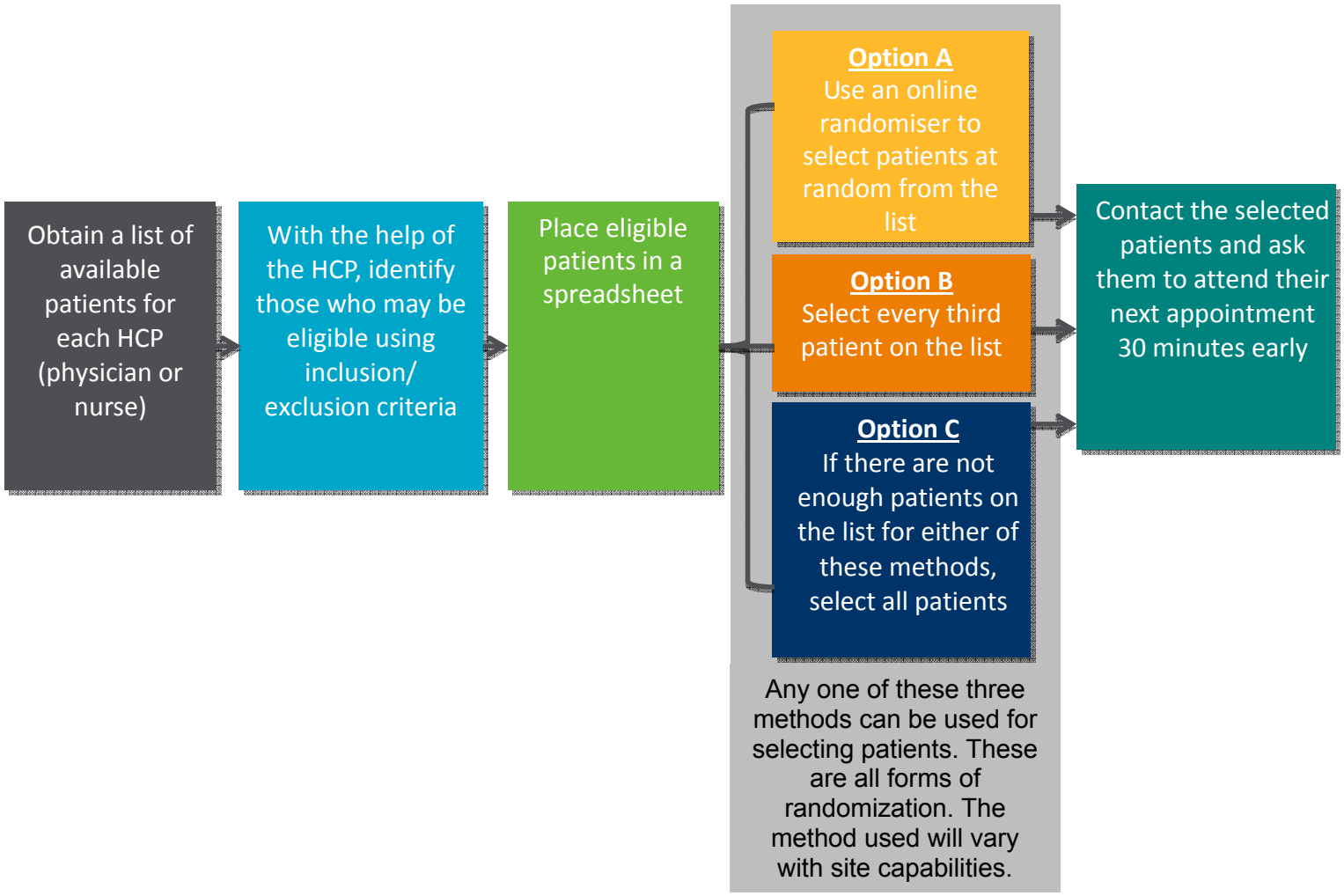
Study Design Schema

Week 1 → Week 39

	Pre-MACPT tool exposure			MACPT tool exposure			
	Standard-of-care- routine visit 1			Standard-of-care routine visit 2			
Prior to all consultations	Before consultation	During consultation	After consultation	Before consultation	During consultation	After consultation	Following all consultations
1. HCP (physician or nurse) and site nurse identify suitable patients using one of the methods outlined in section 10.1 and the eligibility criteria detailed in section 10.3.1.1	1. Patient arrives early and gives **informed consent** and completes a **demographics form** (helped by the site nurse if required)	1. Patient and HCP have face-to-face consultation as per usual practice, not using the MACPT tool	1. HCP completes the **BPI** and **a 5-point VRS** to assess overall pain experience	1. Patient arrives 30 minutes early	1. Patient and HCP have face-to-face consultation. Patient gives **completed MACPT tool** to the HCP and this identifies key discussion points	1. HCP completes the **BPI** and a **5-point VRS** to assess overall pain experience	1. HCP completes **questionnaire assessing usefulness** of the tool
2. Site nurse contacts eligible patients asking them to attend their next Standard of Care (SoC) routine consultation 30 minutes early	2. HCP or site nurse completes **a case report form (CRF)** outlining patient clinical characteristics and the perceived interpersonal **closeness scale** (PICSAppendix J)		2. Patient and HCP complete **consultation satisfaction questionnaire** separately after the consultation	2. The site nurse explains the MACPT tool and the patient completes the tool.		2. Patient and HCP both complete the PICS and the **consultation satisfaction questionnaire** separately to one another	2. Site nurse ensures study documents have been sent to Adelphi Values
	3. Patient completes the **BPI** and a **5-point VRS** to assess overall pain experience, and the **PICS**		3. Patient and HCP both complete PICS	3. Patient completes the **BPI** and a **5-point VRS** to assess overall pain experience, and the **PICS**		3. Patient completes the **questionnaire assessing usefulness**	
			4. Site nurse completes **visit information form**	4. HCP completes the **PICS**		4. Site nurse completes **visit information form**	

Start of study (Consent) — 2 months gap (Max) — End of individual patient enrolment — End of study

Schematic of patient identification and enrolment tasks to be conducted by the site nurse:



*Note. No information that carries the risk of identifying patients will be shared. For example, the online randomizer will use anonymous patient ID codes. The patient's codes will only be presented alongside corresponding identifiable information within a site nurse ledger. This is a password protected spreadsheet that can only be accessed by the site nurse and HCP

1. Table of Contents

2. List of appendices

3. List of Abbreviations

Term	Definition
BPI	Brief Pain Inventory
CRF	Case Report Form
DMP	Data Management Plan
EMA	European Medicines Agency
FAS	Full Analysis Set
HCP	Healthcare Practitioner
ICC	Intraclass Correlation Coefficient
ICF	Informed Consent Form
IEC	Independent Ethics Committee
IQR	Interquartile Range
IRB	Institutional Review Board
MACPT	Managing Advanced Cancer Pain Together
PiMS	Partnership in the Metastatic Setting
PSQ	Patient Satisfaction Questionnaire
SAE	Serious Adverse Events
SD	Standard Deviation
SoC	Standard of Care
VRS	Verbal Rating Scale

4. Responsible Parties

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5. Abstract

Study Title: Assessment of 'Managing Advanced Cancer Pain Together' (MACPT) tool to facilitate communication on total cancer pain between advanced cancer patients and their healthcare professionals.

Study Background and Rationale: It is widely accepted that the experience of pain in cancer has a large impact on quality of life,[1] and the relief of pain has emerged as a priority in oncology care. Pain is associated with the treatments as well as the disease itself, and management is essential from the onset of early disease through long-term survivorship or end-of-life care. Although reports vary widely, the range of reported prevalence of pain is highest for tumours relating to prostate (56–94%), genitourinary (58-90%), breast (40–89%), pancreatic (72-85%)[2] and lung (47%).[3] The prevalence of pain in cancer is estimated at 50% for those following diagnosis in the early stages of the disease, increasing to over 75% for those with advanced disease.[2]

Amgen has set up a steering committee consisting of clinical experts and patient advocates in the metastatic cancer settings; the Partnership in the Metastatic Setting (PiMS). Within PiMS, a subteam of cancer pain specialists from the United Kingdom, France, Germany and Belgium, has been established – the Managing Advanced Cancer Pain Together (MACPT) team. The MACPT team, a multi-professional group of cancer pain management specialists, have drawn on their expertise and current best practice guidelines and developed a simple paper-based conversation tool for use in routine clinical practice, along with input from other HCPs and patients. The MACPT conversation tool is designed to facilitate a comprehensive pain dialogue between cancer patients and their HCPs.[4] The tool is a collection of 41 terms to describe the patient's experience of pain. Each descriptor of pain is based on a biopsychosocial model of pain[4]: physical pain, social pain, emotional pain and spiritual pain. This is supported by the concept of "total pain" which also describes the all-encompassing nature of pain[5]. Patients are asked by their HCP to select three words that best describe their experience of pain. HCPs then encourage patients to explain their choices in order to start a dialogue about the patient's total pain experience, thereby providing a holistic assessment of pain.

Research Question and Objective(s):

- **Primary Objective**

- To assess the impact of the MACPT tool on patient- and HCP- reported overall satisfaction score (as measured using the patient- and HCP- versions of the satisfaction questionnaire) of their conversation during face-to-face routine standard-of-care (SoC) consultations.

- **Secondary Objectives**

  - To assess the impact of the MACPT tool on patient- and HCP- reported satisfaction score (as measured using the patient- and HCP- versions of the satisfaction questionnaire) on specific aspects of their conversation during face-to-face routine SoC consultations
  - To describe the frequency of the tool words selected by the patients as a proxy for elucidating the themes or components of total cancer pain discussed during the face-to-face SoC consultation
  - To assess the usefulness of the MACPT conversation tool in helping HCPs identify key aspects of the patient's total pain experience during the face-to-face SoC consultation from both the patient and HCP perspective

- **Exploratory Objectives**

  - To evaluate the change in levels of concordance between patients' rating of their overall pain experience and HCP's rating of the perceived overall pain experience of the patients before and after use of the MACPT tool
  - To evaluate the change in levels of concordance between patients' reporting of the aspects of total pain that concern them, and HCP's reporting of the patients' concerns before and after use of the MACPT tool
  - To describe the patient-physician relationship from the HCP and patient perspective prior to and after each visit (as measured by the Perceived Interpersonal Closeness Scale (PICS)).
  - To assess the impact of the MACPT tool on patient- reported and HCP-reported overall satisfaction score (as measured using the patient- and HCP- versions of the PSQ) of their conversation during face-to-face routine SoC consultations taking into consideration the patient- and HCP-reported perceived closeness, as measured by the PICS .

- To describe the baseline clinical and treatment characteristics of cancer patients included in the study, including use of therapies for pain relief, use of bisphosphonate or denosumab (XGEVA) therapy for the prevention of skeletal-related events.

- Hypothesis(es)/Estimation:
  - This study will perform significance testing to assess the impact of the MACPT tool on HCP and patients' satisfaction with the conversation during the face-to-face consultation. Significance testing will also be used to assess some of the exploratory objectives. Other analyses will be purely descriptive.

Study Design/Type: This is a short-term pre-post study design. This study will involve direct exposure of advanced cancer patients and their HCPs (the study participants) to the MACPT conversation tool at one of their routine SoC consultations, and data collection via questionnaire surveys completed independently by the participants before and after exposure to the tool. Of note, HCPs can be a physician or nurse.

Survey questionnaires will be administered to both the participating patients and their HCPs at two visits (V):

- V1: before and after the routine SoC routine visit (prior to exposure to the MACPT tool) [study visit 1]
- V2: before and after a subsequent SoC routine visit where the participants will be exposed to the MACPT conversation tool during the face-to-face consultation, with the same HCP as in V1 [study visit 2], if that second visit occurred within 2 months of enrolment into the study

It is essential that the patient has face-to-face consultations with the same HCP at both study visits. At the end of the study when the HCP has met the targeted quota of patients and completed all corresponding consultations, the HCP will complete a brief questionnaire on the usefulness of the MACPT tool in identifying key aspects of the patient's overall pain experience, and the perceived feasibility of using this tool in routine clinical practice.

Setting: Clinical sites, where the MACPT members are located and which include HCPs treating cancer patients, will be approached to recruit patients through a randomized approach into the study. Sites will be asked to compile a list of potential participants

that are due for a routine SoC visit during the study recruitment period and select patients from a randomly ordered list that has been generated electronically. There are four sites based across UK (2 sites), France (1 site) and Germany (1 site), and each will recruit an equal number of patients. At each participating site, patients will be assessed as per the study eligibility criteria. Cancer patients meeting the study criteria will be enrolled into this study. Recruiting sites will be asked to complete a list of the number of patients they have asked to take part in the study and the number of patients who have declined to take part with the reasons for not wanting to participate.

Patient eligibility criteria:

- Age 18 years or older
- A diagnosis with one of the following primary cancer type: breast cancer, prostate cancer, lung cancer or multiple myeloma
- A record of stage IV, metastatic status, distant spread, or bone pain due to cancer metastases/bone lesion(s), specifically:
    - Patients with breast cancer must be diagnosed with advanced or metastatic disease.
    - Patients with prostate cancer must have a nodal or metastatic condition.
    - Patients with lung cancer must have stage IIIB or stage IV non-small cell lung cancer or advanced small cell lung cancer.
    - Patients with multiple myeloma
- Ability to read, write and understand English, French or German (in accordance with the site he/she has been recruited from)
- Sufficient capabilities to participate in the study (as assessed by the HCP)
- No significant difficulty with hearing, reading or speaking
- No diagnosed memory impairment

Follow up: The study will collect data over two routine consultations scheduled as part of the patients' SoC. There is no planned follow-up for patients upon completion of the study.

Variables: Outcome Variable(s):

- The primary outcome variable will be an indicator of whether a participant (patient or HCP) is satisfied with the face-to-face consultation, before and after exposure to the MACPT conversation tool.

Data Sources: This is a non-interventional study in which data collected derive from routine clinical care. Patients and HCPs will complete standardized data collection forms.

Study sample size: The target sample size is 199 patients, based on a calculation using a two-sided paired t-test to assess if the mean change in patient-reported overall satisfaction before and after use of the MACPT tool differs from zero. A small effect size is specified as a conservative effect and is based on Cohen's d effect size[6] rather than being based on prior research or formal hypotheses. Specifying a power of 80%, a small effect[6] size of 0.2 and significance level of 0.05, 199 patients are required for the test to detect a statistically significant effect. At each participating site, approximately two to three HCPs will participate in the study by recruiting patients and taking part in the data collection. The number of participating HCPs at each site will be dependent on the number of eligible HCPs available at each site.

Data analysis:

- The analytic focus will be on pre- and post- MACPT tool exposure.
- The primary analysis will entail comparing the mean change in patient-reported' overall satisfaction scores (as measured using the patient-version of the PSQ) of their conversation during face-to-face routine standard-of-care (SoC) consultations before and after use of the MACPT tool; a paired t-test (or equivalent non-parametric tests if the data are skewed) will assess if the mean change differs from zero. The mean change in HCP-reported overall satisfaction score (as measured using the HCP-version of the PSQ) before and after use of the MACPT tool will also be compared in the same manner, and treated as a co-primary endpoint.
- The secondary analyses include comparing the mean change in patient- and HCP- reported satisfaction score (as measured using the patient- and HCP-versions of the satisfaction questionnaire) on specific aspects of their conversation during face-to-face routine standard-of-care (SoC) consultations, calculating the frequency and percentage of patients selecting

each pain descriptor of the MACPT tool. Both patient and HCP's responses to the brief questionnaire on the MACPT tool's usefulness will also be descriptively summarized.

- As an exploratory objective, the concordance between HCP- and patient-reported overall pain experience scores will be assessed and compared before and after use of the MACPT tool. This will also be assessed for aspects of total pain that concern the patient. Concordance will be assessed in terms of inter-rater reliability and agreement. An additional exploratory objective will be to compare the mean change in patients' perceived closeness to the HCP scores before and after use of the MACPT tool; a paired t-test will assess if the mean change differs from zero. An adjusted analysis will also be conducted to compare the mean change in patients' satisfaction before and after use of the MACPT tool adjusting for the closeness of the patient to the HCP. This analysis will compare the mean change in patients' overall satisfaction scores before and after use of the MACPT tool adjusting for the perceived closeness of the patient to the HCP; a paired t-test (or equivalent non-parametric tests if the data are skewed) will assess if the mean change in satisfaction differs from zero. The change in HCP's overall satisfaction scores will also be compared in the same manner adjusting for the perceived closeness of the HCP to the patient, as measured by the PICS.
- Finally, baseline clinical and treatment characteristics will be descriptively summarized.

6. Amendments and Updates

None

7. Milestones

Milestone	Planned date
Start of data collection	Q1 2018
End of data collection	Q3 2018
Final results presentation	Q4 2018 -Q1 2019
Final report of study results	Q4 2018 -Q1 2019