ENHANCING MULTIDISCIPLINARY INVOLVEMENT IN PERSISTENT SEVERE CANCER PAIN MANAGEMENT: A COLLABORATIVE EUROPEAN APPROACH

Denis Dupoiron,¹ María Luz Padilla,² Rita Kortbaoui,³ Christophe Perruchoud,⁴ Matthew Brown,⁵ Christoph Hoefing,⁶ Vittorio Guardamagna,⁷ Carlos Tornero,⁸ Teresa Macarulla,⁹ Monica lorfida,¹⁰ Mario Di Palma,¹¹ Debora Van Keulen,¹² Somnath Bagchi,¹³ Alejandro Falcon,¹⁴ Xander Zuidema¹⁵ ¹Anesthesiology and Pain. Institut de Cancérologie l'Ouest (ICO), Angers. France; ²Anesthesiology. La Tour Hospital, Geneva. Switzerland; ⁵Pain Medicine. The Royal Marsden Hospital, London. UK; ⁶Pain Medicine. Kemperhof Day Clinic Pain Therapy, Koblenz. Germany; ⁷Palliative Care and Pain Therapy. IEO Hospital, Milan. Italy; ⁸Anesthesiology. Valencia University Hospital, Milan. Italy; ¹⁰Oncology. Valencia University Hospital, Valencia. Spain; ⁹Oncology. Vall d'Hebrón Hospital, Milan. Italy; ¹⁰Oncology. Vall d'Hebrón Hospital, Barcelona. Spain; ¹⁰Oncology. IEO Hospital, Milan. Italy; ¹⁰Oncology. Vall d'Hebrón Hospital, Milan. Italy; ¹⁰Oncology. Vall d'Hebrón Hospital, Barcelona. Spain; ¹⁰Oncology. Vall d'Hebrón Hospital, Barcelona. Spain; ¹⁰Oncology. Valencia University Hospital, Valencia. Spain; ¹⁰Oncology. IEO Hospital, Milan. Italy; ¹¹Oncology. Custave Roussy Hospital, Valencia. Spain; ¹⁰Oncology. Vall d'Hebrón Hospital, Milan. Italy; ¹⁰Oncology. Valencia. Spain; ¹⁰Oncology. Vall d'Hebrón Hospital, Milan. Italy; ¹⁰Oncology. Valencia. Spain; ¹⁰Oncology. Valencia. Spain hospital, Utrecht. Netherlands; ¹³Anesthesiology and Pain Medicine. Plymouth Hospitals NHS Trust, Plymouth. UK; ¹⁴Oncology. Virgen del Rocío Hospital, Seville. Spain; ¹⁵Anesthesiology. Diakonessenhuis Zeist Hospital, Zeist. Netherlands.

Background and objectives

Pain is the commonest symptom in patients with cancer at diagnosis, whose prevalence can vary between 30-70% throughout the stage of disease.^{1,2} Despite pain being a frequent symptom, undertreatment is usual, and just one in three patients do not receive appropriate analgesia.² Uncontrolled or undertreated pain may lead to increased suffering and reduced quality of life $(QoL).^1$

Real world practice often shows that the majority of patients experiencing cancer pain are referred too late to the Pain specialists' units, therefore time is specifically challenging to ensure they could benefit from recognized therapies that have demonstrated outcomes in cancer pain analgesia.^{3,4}

This study aimed to develop a comprehensive set of recommendations for the multidisciplinary management of persistent severe cancer pain, based on the usual clinical practice and the opinion of experts in the field from across Europe.

Materials and methods

The study encompassed two phases with two parallel scientific committees of pain specialists and oncologists (Figure 1):

- Phase 1: The pain scientific committee developed a clinical practice survey regarding the management of persistent severe cancer pain in Western Europe which was then validated by the oncologist scientific committee.
- Phase 2: Based on the survey results the pain scientific committee helped identify controversies in the management of cancer pain in the clinical environment and proposed a pool of recommendations that was then discussed and agreed in a European consensus meeting within the two scientific committees.

The survey included 19 questions on 6 topics: 1. Perceptions and clinical relevance of cancer pain; 2. Diagnosis and assessment; 3. Management with conventional therapies; 4. Management with interventional therapies; 5. Follow-up; 6. Referral to a pain unit. The survey was distributed to oncologists at the start of July, with the data cut-off set for October 18th. Seventy-seven European (from France, Spain, Netherlands, Italy, United Kingdom, and Germany) medical oncologists with ≥ 5 years of post-residency experience completed the survey.

Fifteen recommendations were then proposed and agreed by a joint expert meeting of the two committees by means of the Delphi-like methodology, using a 9-point rating scale (1=completely disagree and 9=completely agree). Responses were grouped by terciles: 1-3 disagreement, 4-6 indeterminate, 7-9 agreement. Consensus on a recommendation was reached when \geq 75% of the participants were in the same tercile (Figure 2).

Figure 1: Project's overview.

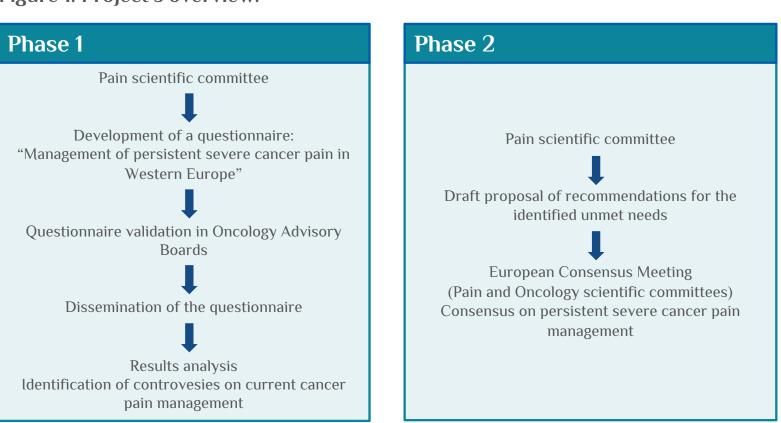
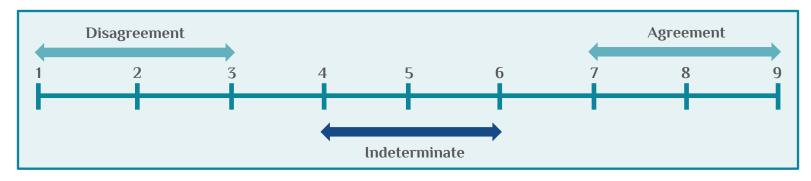


Figure 2: Level of agreement and threshold required to reach consensus. Consensus: \geq 75% of response in the same tercile.



Results

The panel of experts consisted of fifteen experienced pain specialists and oncologists from across Europe. Internal consistency of the questionnaire was high (Cronbach's alpha 0.776, p<0.001) (Table 1).

After two rounds of Delphi-like, consensus was obtained in 13 recommendations (81.25%) regarding the collaboration between both specialties, training on cancer pain for oncologists, and referral criteria (Table 2).

 Tabla 1: Survey consistency

	Rou	nd 1	Round 2		
	Cα (p)	ICC (p)	C α (p)	ICC (p)	
TOTAL (15 and 16 items in first and second round, respectively)	0.780 (<0.001)	0.767 (<0.001)	0.776 (<0.001)	0.774 (<0.001)	

The validity of the questionnaire was assessed using Cronbach's alpha test (C α). The value of C α ranges from 0 to 1, where values closer to 1 indicate higher reliability. A C α value of 0 suggests no reliability, while a value of 1 signifies maximum reliability. Values above 0.7 are deemed acceptable for research purposes, those between 0.7 and 0.9 are considered to have high reliability, and values exceeding 0.9 indicate very high reliability. The intraclass correlation coefficient (ICC) is also calculated as a measure of reliability with the interpretation like $C\alpha$, the values of the first and second round are shown.

References: 1. Bennett MI, et al. Standards for the management of cancer-related pain across Europe-A position paper from the EFIC Task Force on Cancer Pain. Eur J Pain. 2019;23(4):660-668; 2. Fallon M, et al. Management of cancer pain in adult patients: ESMO Clinical Practice Guidelines. Ann Oncol. 2018;29(Suppl 4):iv166-iv191; 3. Perruchoud C, et al. Management of cancer-related pain with intrathecal drug delivery: a systematic review and meta-analysis of clinical studies. Neuromodulation. 2022;S1094-7159(21)06969-5; 4. Breivik H, et al. Cancer-related pain: a pan-European survey of prevalence, treatment, and patient attitudes. Ann Oncol. 2009;20(8):1420-33.

Conclusions

Experts agreed that comprehensive cancer pain management requires enhanced collaboration between specialties, targeted education on cancer pain management provided by pain physicians to oncologists and/or palliative care specialists, and the co-creation of local protocols with clear patient selection criteria to facilitate accurate and timely referrals to pain specialists. These steps are essential to ensure patients have access to appropriate treatments.

Table 2: Recommendations and Delphi-like result

Nº	Recommendation	1 st round results	Decision	New rephrased	2 nd round results	Final result	Scope
1	A Pain specialist should attend the tumor board for the assessment of patients with persistent severe cancer pain.	NC-D 9 (60%) [1-3]; 4 (27%) [4-6]; 2 (13%) [7-9]	To be deleted			NC-D	
2	Specific committees for cancer pain treatment should be created in those centers where a tumor board is not available.	C-A 1 (7%) [1-3]; 2 (13%) [4-6]; 12 (80%) [7-9]	To be rephrased	Specific committees for cancer pain treatment should be created in all centers treating cancer patients.	C-A 2 (13%) [1-3]; 0 (0%) [4-6]; 13 (87%) [7-9]	C-A (87%)	Collaboration & communication
3	Telematic consultation (e.g.: online meetings, internal chat, phone) on cancer pain between oncologists and Pain specialists should be put into practice.	C-A 0 (0%) [1-3]; 0 (0%) [4-6]; 15 (100%) [7-9]				C-A (100%)	Education & Training
4	All cancer patients with pain should be seen at least once in a Pain Unit, when available, as part of their comprehensive cancer care.	NC-A 4 (26%) [1-3]; 4 (27%) [4-6]; 7 (47%) [7-9]	To be deleted			NC-A	
5	The Medical Oncology service and the Pain Unit of a center should have common protocols for treating and referring patients to the Pain Unit.	C-A 0 (0%) [1-3]; 0 (0%) [4-6]; 15 (100%) [7-9]				C-A (100%)	Collaboration & communication
6	Clear-cut referral criteria (e.g.: clinical characteristics, non-clinical criteria, life expectancy) should be established to timely refer patients to the Pain Unit and avoid delays in patient management circuits.	C-A 0 (0%) [1-3]; 0 (0%) [4-6]; 15 (100%) [7-9]				C-A (100%)	Referral
7	Pain Units should organize update sessions on cancer pain management, including guidelines/protocols, cases/ RWE and outcomes of the available interventional techniques.	C-A 0 (0%) [1-3]; 0 (0%) [4-6]; 15 (100%) [7-9]				C-A (100%)	Education & Training
8	Training sessions for medical oncologist should include guidance on the appropriate patient profile for interventional techniques.	C-A 1 (7%) [1-3]; 2 (13%) [4-6]; 12 (80%) [7-9]				C-A (80%)	Education & Training
9	Patients with tumors frequently associated with severe pain (such as head and neck, pancreatic, bone and lung cancer) should be always referred to the Pain Unit for assessment.	NC-A 3 (20%) [1-3]; 2 (13%) [4-6]; 10 (67%) [7-9]	To be rephrased	A patient should be referred to the Pain Unit for assessment if pain is an initial symptom, especially in cancers that are frequently associated with pain.	C-A 1 (7%) [1-3]; 2 (13%) [4-6]; 12 (80%) [7-9]	C-A (80%)	Referral
10	Patients with relevant comorbidities (as defined by the tumor board) should be referred to the Pain Unit for assessment.	NC-l 3 (20%) [1-3]; 6 (40%) [4-6]; 6 (40%) [7-9]	To be rephrased	Patients with relevant comorbidities that can interfere with pain treatment should be referred to the Pain Unit for assessment.	NC-A 1 (7%) [1-3]; 3 (20%) [4-6]; 11 (73%) [7-9]	NC-A	
11	Patients with poor QoL due to persistent severe cancer pain should be referred to the Pain Unit for assessment.	C-A 0 (0%) [1-3]; 0 (0%) [4-6]; 15 (100%) [7-9]				C-A (100%)	Referral
12	Patients with persistent severe cancer pain should be referred to the Pain Unit regardless of the pain localization (local, diffuse, global).	C-A 0 (0%) [1-3]; 0 (0%) [4-6]; 15 (100%) [7-9]				C-A (100%)	Referral
13	Patients with persistent severe cancer pain should be referred to the Pain Unit regardless of the presence of chemotherapy-related AEs.	C-A 0 (0%) [1-3]; 0 (0%) [4-6]; 15 (100%) [7-9]				C-A (100%)	Referral
14	Patients with persistent severe cancer pain should be referred to the Pain Unit regardless of the presence of AEs from conventional pain treatment.	C-A 1 (6%) [1-3]; 1 (7%) [4-6]; 13 (87%) [7-9]				C-A (87%)	Referral
15	For appropriate patients, early communication on pain management and the role of a Pain Unit should be addressed as a key driver in their QoL.	C-A 1 (6%) [1-3]; 1 (7%) [4-6]; 13 (87%) [7-9]				C-A (87%)	Collaboration & communication
16			New added	All centers treating cancer must have access to a Pain management specialist.	C-A 0 (0%) [1-3]; 1 (7%) [4-6]; 14 (93%) [7-9]	C-A (93%)	Collaboration & communication

AE: adverse event; C-A: consensus-agreement; NC-A: no consensus-agreement; NC-D: no consensus-disagreement; NC-l: no consensus-indeterminate; QoL: quality of life; RWE: real world experience.