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**Developing a decision support tool for the continuation or deprescribing of antithrombotic therapy in patients receiving end-of-life care: Results of a European Delphi study**

For the DELPHI Serenity Group

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## Highlights

- A Delphi process was initiated with multidisciplinary European experts.
- Experts explored antithrombotic treatment (ATT) deprescribing in end-of-life cancer care.
- The study builds consensus on informed decision-making and support requirements.
- Optimal timing for considering ATT deprescribing might be 3-month prognosis.
- Palliative care specialists, oncologists, general practitioners are the deprescribing deciders.

## **ABSTRACT (249 / 250 WORD)**

**Introduction:** To develop a European shared decision-support tool (SDST), a two-round Delphi process was used to achieve consensus on aspects relating to the antithrombotic therapy (ATT) deprescribing discussions and process in end-of-life cancer patients.

**Methods:** Conducted between September 2024 and March 2025, the Delphi survey was developed by a multidisciplinary 24-member steering committee (SC), including medical specialists in oncology, hematology, palliative care, primary care, geriatrics, and vascular medicine. The survey involved 188 experts from these specialties across eight European countries. Consensus was defined with pooled items as  $\geq 70\%$  agreement with a final decision by the SC. Themes covered deprescribing timing, stakeholders, reassessment and clinical drivers of patients with ATT, SDST, and choice of outcomes for a randomized controlled trial (RCT) to evaluate the SDST.

**Results:** Round 1 reached consensus for seven pooled questions (37%), especially the reassessment of ATT deprescribing. Considering these results, the SC reformulated round 2 to reduce ambiguity and move toward consensus. The SC made the final decision. Three medical specialties should be involved in ATT deprescribing: palliative care specialists, oncologists, and general practitioners after a triggering circumstance such as clinical triggers or at 3-month prognosis. For the SDST design, the findings confirmed that this tool would be meaningful to clinicians. Eleven predefined outcomes were selected for a future RCT.

**Conclusion:** These results succeeded in shaping the content of the future CoClarity SDST and mapping its useability in palliative care clinical pathways across Europe, with the perspective to support informed decision-making, reduce complications, and improve quality of life in this population.

## INTRODUCTION

Thanks to progress in anticancer treatments and supportive care, patients with cancer have an improved life expectancy, including those with advanced cancer (1). Given these trends, increasing numbers of cancer patients are managed in daily care for increasing periods of time. Consequently, the care pathway for these patients is evolving, and many health care professionals (HCPs) and medical specialties are involved during the course of their treatment, including physicians, pharmacists, nurses, and psychologists (2).

Despite the substantial risk of bleeding and impaired quality of life for cancer patients receiving antithrombotic therapy (3–6) (ATT) at the end of life, continuing ATT is common in practice (7–12), questioning the benefit risk ratio of ATT continuation. However, ATT discontinuation is an ongoing matter of debate (13). To address this challenge posed by ATT use in end-of-life cancer patients, the SERENITY (towardS cancer patiEnt empoweRment for optimal usE of aNtithrombotIc TherapY) project was initiated (20,21). By integrating evidence-based data, HCPs' expertise, and patients' preferences, SERENITY aims to implement a European web-based shared decision support tool (SDST) to support patients, their carers/family, and HCPs in making informed decisions about ATT near the end of life.

This ATT discontinuation option is discussed by the HCPs involved in patient care pathway (14,15), in close collaboration with patients and their carers/family.

Previous studies showed that values, views, and preferences can differ between patients (12), (14,18), carers, and HCPs across countries (19) at each step of the deprescribing discussion and decision process. Reaching an individualized consensus on a decision and optimal timing of ATT deprescribing is required, as recommended for patients with advanced cancer (16,17).

The current study, an integral part of the SERENITY project (21,22), aims to achieve consensus across patients, their carers/family, and HCPs on aspects relating to ATT deprescribing in end-of-life cancer patients with the broader objective of contributing to the development, evaluation, and implementation of the SERENITY SDST.

## **METHODS**

### **Study Design and Reporting Standards**

We conducted a European Delphi consensus study to develop recommendations on the deprescription or continuation of ATT in patients with advanced cancer at the end of life. SERENITY was structured around seven work packages (WPs) as WP4 consensus-building processes to inform the development of the SDST (23,24)). The study followed the ACCORD (ACcurate COnsensus Reporting Document) guidelines for the SDST (23,24) for consensus-based biomedical research and the CREDES (Conducting and REporting of DElphi Studies in palliative care) standards to ensure methodological transparency and relevance to palliative care.

The detailed description of the study design and the development of the Delphi form can be found in the published protocol (23). It was approved by the North AP-HP ethics committee (IRB 00006477- CER-2024-294).

### **Steering Committee and Panel**

The Delphi process was coordinated by the SERENITY WP4 steering committee (SC), a multidisciplinary group comprising 24 experts from eight European countries (Denmark, France, Germany, Italy, Netherlands, Poland, Spain, and United Kingdom) involved as the leaders or investigators in the SERENITY project. Their roles were threefold: to define the

panel composition, to coordinate the recruitment of the expert panel for their country, and to validate the results of the two rounds and final consensus.

The expert panel was likewise multidisciplinary and multicountries to ensure a holistic perspective, being structured into three groups: (1) physicians prespecified as being mainly involved in ATT decision-making, defined as experts in oncology, palliative care, cardiology, and primary care; (2) physicians prespecified as being potentially involved, defined as medical specialists in geriatrics, hematology, vascular medicine, vascular surgery, neurology, and respiratory medicine; and (3) other HCPs (e.g., pharmacists, nurses, psychologists). Participants were required to preregister by giving their agreement and, at the same time, they were asked to complete the study form relating to the expert panel characteristics.

### **Development of the Delphi Form**

Delphi items were informed by findings from the SERENITY project WP1-3 (realist review, flash mob research, epidemiological and qualitative studies) (4–6,10,11,14,18,19,21,25,26) and refined by the SC, with the additional input of patient and public involvement representatives.

The form comprised four sections: (1) guidance for the SDST addressing patient and health care team characteristics (stakeholders) regarding the timing and modalities of reassessment (3 parts with 9 questions for 97 items); (2) clinical drivers for the SDST (1 question for 22 items); (3) SDST design (8 questions for 41 items); and (4) expected candidate outcomes for the SDST RCT (1 question for 16 items). Delphi items provided a wide range of information on the clinical and social factors to be taken into account when considering the continuation or deprescription of ATT.

In round 1, participants evaluated each item using five-point Likert-like scales (from “Not Important” to “Essential”), binary yes/no responses, or ranking methods depending on the

nature of the question. Free-text boxes allowed participants to provide comments and suggest additional items. The complete Delphi form can be found in Supplementary Material (SM1).

### **Assessing consensus**

The Delphi process was conducted over two rounds with a final validation by the SC. All the responses were collected anonymously using a dedicated electronic tool with controlled access.

#### **Interpretation of round 1**

Options with answers in the form “Not important / Less important / Moderately important / Important / Essential” were interpreted as consensual if Important and Essential had at least 70% of answers (consensus in favor) or if Not important and Less important had at least 70% (consensus against). Other options were considered not to have reached consensus. Marginal cases could be resolved with numeric scoring in the first or last tertile, as recommended in Delphi interpretations.

Ranking of the required information used an alternate voting system to aggregate individual rankings. To find the most important option, the modality with the fewest first-place preferences was eliminated, thus moving up the remaining modalities in each individual ranking; then the next modality with the fewest first-place preferences was eliminated, and so on until only one remained. Once the most preferred option was determined, it was removed from the individual rankings, and the same process was run to find the second most preferred option and so on. Aggregated results were communicated to the panel members in the introductory materials for round 2. Items with a consensus to be included in the SDST were clearly identified, and the level of agreement was indicated. Similarly, items with a consensus to be excluded were highlighted along with the reasons for their exclusion.

## Reformulation for round 2

Round 2 was based on the aggregated results of round 1 that were validated by the SC during a dedicated meeting (Supplementary Material SM2). Items reaching consensus for inclusion or exclusion were highlighted, while those without a clear consensus were reformulated for further clarification. Because it was apparent that the concept of “Important” meant different things to different respondents, questions were reformulated in a more direct manner, with modalities adapted to each question. For questions relating to the relevant stakeholders, responses related to the appropriateness of their participation at each step and whether their participation was indispensable or not.

Final results from each round were shared with participants in an anonymized summary form.

## Final consensus

Instead of initiating a complete round 3, the SC validated the final consensus during a dedicated meeting. The final process was proposed based on the level of consensus reached in round 2 while noting the same elements in the gray area across the two rounds.

## Data analysis

Responses from rounds 1 and 2 were analyzed by the lead team with a dedicated team blinded to the identity of the expert panel. Quantitative and qualitative analyses were performed. Descriptive statistics such as response rates, level of agreement for each item, mean levels of agreement, and standard deviations were used to describe agreement rates between rounds. The same measurements were used to evaluate consensus stability across rounds (23).

Qualitative analysis examined the comments and suggestions provided by experts, with identified patterns presented alongside the statistical summary for each corresponding item.

## RESULTS

## **Delphi Panel composition**

Recruited by each SC country leader, 247 experts were invited to participate in the Delphi process. Round 1 was open from September 30 to November 8, 2024. A total of 188 (76%) experts responded fully (167 – 68%) or partially. The expert panel comprised 54.3% of women; the mean age was 47.4 ( $\pm 9.9$ ) years, and the mean year of certification was 2002 ( $\pm 13$ ). Overall, 66% considered themselves experts; on average, they had 20.8 ( $\pm 9.6$ ) years of experience with a focus on patients with advanced cancer for 81% (frequency defined as exclusively or often). A focus by expertise field and country is detailed in Figure 1. The three main specialties were palliative care (22%), oncology (19%), and cardiology (16%). All the eight countries were represented. The Delphi form for round 2 was developed based on the round 1 results approved by the SC. This round ran from February 10 to March 21, 2025. Of the 188 experts who completed round 1 and were sent a new dedicated link for the questionnaire of round 2, 129 (69%) began it and 117 (62%) completed it (no significant differences were observed within the expert group between the two rounds; Figure 1).

Results are shown in Figure A3 with six main themes for the four sections: timing, stakeholders, and reassessment for section 1; clinical drivers for section 2; SDST design for section 3; and outcomes for section 4. The complete process of this European Delphi study for the round 3-like decision made by the SC is presented in Figure 2, with the SC's final opinion presented in Table 1.

### **Timing**

Considering the timing theme, for the question “When is it the most appropriate to consider initiating discussion on antithrombotic deprescribing?”, 89% of the panel chose at the event of triggering circumstances such as clinical triggers.

For the reformulated round 2 question “In addition to triggering circumstances, should the following prognosis time points be systematically used to initiate a multidisciplinary discussion about antithrombotic deprescribing?” the expert panel gave a higher agreement rating for the 3-month prognosis than for the 6-month prognosis (Figure A3.A).

### **Stakeholder**

Of the five questions relating to the stakeholder theme, all needed to be reformulated for round 2. Three items obtained consensus pooling (Essential or Important) for the question “What situations do you think should trigger discussions about antithrombotic treatment discontinuation?”: patients with a perceived high risk of bleeding (90% agreement, score  $4.5 \pm 0.8$ ); patients expressing a desire to stop antithrombotic treatment (agreement 87%, score  $4.5 \pm 0.8$ ); and patients experiencing persistent low platelet counts (agreement 78%, score  $4.1 \pm 1$ ) (Figure A3.B).

To finalize the list of stakeholders initiating the discussion on ATT prescribing, as defined after round 1, the panel of experts decided to include the following specialties: geriatrician, internist, cardiologist, hematologist, home hospitalization physician, and general practitioner. Caregivers/families and nurses were excluded from this list.

Four specialties, which remained in the gray area, should be proposed at the final decision by the SC. Similar results were observed for the list of stakeholders with a primary role in the ATT deprescribing decision and who should be informed about the ATT deprescribing (Figure A3.B).

### **Reassessment**

For the reassessment theme, all items achieved a consensus rate at round 1. The first question (“The decision regarding antithrombotic treatment deprescribing should be reassessed”) was rated as Essential or Important by 76% of respondents ( $4.1 \pm 0.8$ ). The question “When should

the patient's preference regarding antithrombotic treatment deprescribing be reassessed?" had three positive consensus results: on the occasion of an intercurrent event (agreement 86%, score  $4.4 \pm 0.8$ ); when the patient's family requests a reassessment (agreement 87%, score  $4.4 \pm 0.8$ ); and during follow-up visits (agreement 80%, score  $4.1 \pm 0.8$ ). One negative consensus (Less important or Moderately important) was achieved for the response of every 4 weeks (agreement 67%, score  $2.7 \pm 1$ ). Positive consensus for the question "When should a reassessment of the decision be scheduled if the initial decision is not to stop antithrombotic treatment?" was achieved in the case of patients changing preference, triggering circumstances as such clinical triggers, and during follow-up visits (Figure A3.C).

### **Clinical drivers**

The five most important factors that should influence ATT deprescribing as rated by the expert panel were: (1) perceived high bleeding risk; (2) patient preference to stop ATT; (3) persistent low platelet count; (4) estimated benefit–risk balance; and (5) cancer progression while on cancer treatment. However, consensus was not reached, so a binary response option was proposed: "required" or "optional" (Figure A3.D).

Based on a dichotomized modality of "required" or "optional" responses, the list of the clinical drivers needed to make an appropriate ATT deprescribing or continuation decision at the >70% threshold included the first five factors selected in round 1: perceived high bleeding risk (100%), patient preference to stop ATT (97%), persistent low platelet count (97%), estimated benefit–risk balance (97%), cancer progression while on cancer treatment (95%), estimated life expectancy (93%), deterioration in quality of life (91%), anticancer drug discontinuation (85%), and high risk of falls (76%) (Figure A3.D).

## **SDST design**

Three of the eight questions relating to the SDST design theme reached a positive consensus. For the question “When using the shared decision-support tool, clinicians should engage in a discussion with the patient and/or their carer/family,” all six items were positively rated by the expert panel, confirming that the discussion should focus on the indication and objectives of ATT, adverse events, clear explanations in favor of ATT discontinuation, anticipated outcomes after discontinuation, motivation for discontinuation, ATT deprescribing, and pharmacological interactions. According to the expert panel, patient-specific use involves focusing on targeted access to patient information and SDST design results (Essential or Important for 74%;  $3.9 \pm 0.9$ ). The final questions with a positive consensus related to the content to help guide a clinical decision: (1) treatment options for a specific patient situation (e.g., age, sex, weight, clot history) to predict the personalized risks and benefits of ATT at a rate of 85% ( $4.2 \pm 0.7$ ); and (2) selecting viable treatment options from a list provided in the tool for clinicians at a rate of 82% ( $4.1 \pm 0.7$ ). The other questions were reformulated and rated once again in round 2 (Figure A3.E).

Round 2 did not succeed in reaching a consensus to validate the use of the following four items in the list of collected information in the SDST: carer/family health literacy, cultural and religious values, socioeconomic context, and patient health literacy. Consistent round 1 cycle identified clinicians involved in discussions and decision-making as the HCPs targeted by the SDST. However, this second cycle did not result in a consensus being reached for other clinicians involved in the patient’s care pathway such as nurses and pharmacists (Figure A3.E).

## **Outcomes**

Eleven of the sixteen predefined outcomes for the RCT were selected by consensus for inclusion in the clinical trial, namely, major bleeding, symptomatic pulmonary embolism, symptomatic

deep vein thrombosis, stroke, arterial or venous thromboembolism, quality of life, myocardial infection, composite of bleeding and thrombosis, composite outcome including bleeding and thrombosis, patient and clinician satisfaction with the SDST tool. A confirmation of the consensus to omit the four other predefined outcomes was proposed in the round 2 (Figure A3.F).

Minor bleeding was rated by the expert panel as a primary candidate outcome for the RCT, although four predefined outcomes were always in the gray area: psychological symptom assessment, preferred place of care, health economics, and time spent at home.

#### **Final decision by the steering committee**

Three medical specialties were endorsed as the main medical drivers of ATT deprescribing: palliative care specialists, oncologists, and general practitioners. This same trio of HCPs was attributed the primary responsibility for ATT deprescribing. However, all the relevant stakeholders should be consulted, especially the patient's family, nurse, and initial prescriber. The SC confirmed the relevance of the first list of clinical drivers established in round 1 and completed with six items positioned in the gray area in round 2: low thrombotic risk, medication burden, oral route difficulty, performance status, drug-drug interactions, and subcutaneous difficulty. The SC expressed that this list should be collected before the multidisciplinary meeting. For the SDST design, the SC confirmed that, most importantly, this tool should be meaningful to the concerned clinicians in contrast to patients. It should not include patient health literacy, carer health literacy, cultural/religious values, and socioeconomic context. These four outcomes rated in the gray area were identified by the SC as secondary trial candidate outcomes, indicating a lack of discrimination on the part of Delphi.

## DISCUSSION

This Delphi Study is the first study to establish an international consensus about the ATT deprescribing discussions and processes across different HCPs involved in the care pathway of advanced cancer patients receiving ATT at the end of life. This is a challenging issue, considering the associated risk of bleeding and impaired quality of life (3–6) at the end of life, and on the other hand the therapeutic inertia surrounding ATT deprescribing in end-of-life cancer patients as well as the disparities across countries, specialties, and patients (14,18,19,25,26).

With the objective of preparing a SDST based on a dynamic and practical deprescription process and facilitating the successful implementation of the pan-European SERENITY intervention in daily practice, the Delphi process was split into successive steps: initiation of the discussion, responsibility for the decision, and decision sharing between HCP, and with patient.

Our study led to the following main findings. First, we confirm a life expectancy of 3 months as the ideal time to consider ATT deprescribing in patients with advanced cancer, which is consistent with the definition of end of life in cancer patients based on the flash mob results from SERENITY WP1 (19). Second, all HCPs ideally could be involved together during discussion process, although oncologists, palliative care specialists, and initial ATT prescribers have a primary and influential role in the ATT deprescribing decision. Notably, HCPs consider the patient's viewpoint and their role in the process to be crucial, thus confirming previous data (14). This may lead to a paradox whereby patients trust HCPs to lead in terms of decision-making and for relatives to play a key supportive role (18). Carers, by contrast, are not identified as playing a key role in the initiation of discussions or the deprescribing decision-making

process. Third, decisions about ATT deprescribing are dynamic, and there is a strong consensus for decision reassessment in different contexts such as complications, patient/carer request, follow-up visits, or physician discretion. Fourth, a major achievement of our study is that it provides a consensus on the determinants of the deprescribing decision: patient-related factors (patient preference, deterioration in quality of life), cancer-related factors, a perceived high risk of bleeding (persistent low hemoglobin, low platelet count, high fall risk), and/or an estimated unfavorable benefit–risk ratio (estimated life expectancy, cancer progression without treatment options, discontinuation of anticancer drugs).

Overall, this study identified key elements for the CoClarity SDST, a web-based tool designed to support patients with cancer, their caregivers, and HCPs to discuss and make an informed choice about ATT (dis)continuation as they approach the last phase of life , according to their values and preferences, together with their physician : namely, identifying the candidates for ATT deprescribing, clarifying the roles of the HCP in the decision-making process, and addressing the specific information and communication needs of patients. Moreover, the Delphi consensus outlined the support tool requirements for SDST development (WP5): the most important items to be aware of for clinicians in charge of the deprescribing decision, the themes to be discussed with patients and carers, and the ways in which the decision should be explained (i.e., helping patients and carers to clearly understand the reasons for and against ATT deprescribing, awareness of discontinuation effects, providing contact information, and encouraging questions).

In addition, this study helped determine to identify a set of candidate outcomes of the RCT, which will evaluate the effectiveness of the tool (SERENITY WP6). This list of 11 candidate outcomes involves a large panel of criteria covering venous and arterial complications, bleeding complications as well as patient and clinician satisfaction with the tool.

Our study has strengths and limitations. One key strength was the large and varied sample of HCPs involved in this Delphi process, with only a minimum threshold. Additionally, it was conducted across diverse European countries and cultural contexts, thus reinforcing the consensus and its potential application to the SDST and in practice. The involvement of each country leader in recruiting the expert panel helped ensure participation and minimize loss to follow-up.

The Delphi form was based on the findings of the previous WPs, including a realist review, flash mob study, large-scale epidemiological research, and qualitative studies, which supported the relevance of the questions addressed to participants (4–6,10,11,14,18,19,21,25,26). The guiding thread was designed both to inform the SDST content and to be applicable in practice.

Another strength of this study is the multidisciplinary expertise of our research team and SC made up of experts from various fields, including public involvement and patient representatives. It was also led by a team with a strong background in Delphi methodologies.

The study also has some limitations. The Delphi questionnaire was written in English, which was not the native language of many participants. However, the question formulation was reviewed by all the country leads, and the questionnaire was tested to guarantee the comprehension of the questions and the reliability of the findings. Due to unbalanced recruitment in certain countries despite compliance with the threshold per country and specialty, the consensus characteristics for each country have not been detailed. The consensus was defined in the study protocol (23) before the start of the study. Some adaptations were needed (<70%), with pooled items of the Likert-like scales and a reformulated version made by the SC for round 2. In addition, three rounds were planned as per the guidelines. According to the objective to reach a consensus, the final decision for the items that were always in the gray area was performed by the SC expert team with a diverse European representation.

As we faced major ethical and legal issues related to patient recruitment across Europe with an extended lead time to obtain regulatory opinions, we decided not to include patients in the Delphi panel. However, patient perspectives were taken into account through the large amount of data collected in the patient interviews (18) as well as the patient and public involvement through advisory contributions to the work of the consortium. These consensus findings must be confirmed among patient groups.

In conclusion, the findings of this Delphi study conducted with specialists from eight European countries succeeded in shaping the content of the future SDST for ATT therapy in end-of-life care by contributing to ensure its usability in palliative care clinical pathways across Europe, with the objectives to reduce complications, improve quality of life in this population, and inform the candidate outcomes in a subsequent RCT testing the CoClarity SDST.

## Tables

**Table 1** Summary of the overall results, including the final decision made by the steering committee

Footnotes: (R2) consensus reached in round 2; DVT, deep vein thrombosis; PE, pulmonary embolism

## Figures

**Figure 1** Panel characteristics by country (A), by frequency of working with end-of-life patients (B), by speciality (C), and by employment status in rounds 1 and 2

Footnotes: Double specialties and specialties outside those shown here were ignored. Palliative care was considered the primary specialty for the context of this survey. Hematology includes onco-hematology. One geriatric cardiologist was categorized as a geriatrician. Contract superseded other employment modes, while full-time then superseded other modes.

**Figure 2** Process of Delphi consensus including the consensus rated in rounds 1 and 2.

Footnotes: Upper part in dark green retained in round 1 and in light green retained in round 2 with a threshold >70%; lower part in bright red rejected in round 1 and in dark red rejected in round 2 with a threshold <30%; and the gray area (30-70%). Interpretation is shown in contrast to other answers. Options shown ranked from the strongest to weakest majority.

## **AUTHOR CONTRIBUTIONS**

All authors participated in the design of the Delphi study and approved the final draft. IM and CC led the writing of the protocol. SN contributed to the regulatory aspects of the study. SH performed the analysis and provided the tables and figures. The steering committee with IM, CC, SH, and SN conceived the questionnaires of rounds 1 and 2.

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## COMPETING INTEREST'S STATEMENT

- IM (Isabelle Mahé) declares grants from BMS Pfizer, and fees for speaker and board and from BMS Pfizer and Leo Pharma, not related to the present work.
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- SN (Simon Noble) holds a Marie Curie Chair in Supportive and Palliative Medicine
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