

Perspectives of the medical oncologist regarding adjuvant chemotherapy for pancreatic cancer: An international expert survey and case vignette study

N.C. Biesma^{a,*}, M.U.J.E. Graus^{b,*}, G.A. Cirkel^c, M.G. Besselink^{d,e}, J.W.B. de Groot^f, B. Groot Koerkamp^g, K.H. Herbschleb^h, M. Los^h, R.C. Verdonkⁱ, J.W. Wilmink^{e,j}, A. Cervantes^k, J.W. Valle^{l,m}, L.B.J. Valkenburg-van Iersel^b, F.E.M. Froelingⁿ, I.Q. Molenaar^a, L.A. Daamen^{a,o}, J. de Vos-Geelen^{b,1}, H.C. van Santvoort^{a,1,*}, for the Dutch Pancreatic Cancer Group

^a University Medical Center Utrecht Cancer Center & St. Antonius Hospital Nieuwegein, Regional Academic Cancer Center Utrecht, Department of Surgery, the Netherlands

^b Maastricht University Medical Center, Department of Internal Medicine, Division of Medical Oncology, GROW, Research Institute for Oncology & Reproduction, Maastricht, the Netherlands

^c University Medical Center Utrecht Cancer Center & St. Antonius Hospital Nieuwegein & Meander Medical Center Amersfoort, Regional Academic Cancer Center Utrecht, Department of Medical Oncology, the Netherlands

^d Amsterdam UMC, Location University of Amsterdam, Department of Surgery, Amsterdam, the Netherlands

^e Cancer Center Amsterdam, the Netherlands

^f Isala Oncology Center, Department of Medical Oncology, Zwolle, the Netherlands

^g Erasmus Medical Center, Department of Surgery, Rotterdam, the Netherlands

^h University Medical Center Utrecht Cancer Center & St. Antonius Hospital Nieuwegein, Regional Academic Cancer Center Utrecht, Department of Medical Oncology, the Netherlands

ⁱ University Medical Center Utrecht Cancer Center & St. Antonius Hospital Nieuwegein, Regional Academic Cancer Center Utrecht, Department of Gastroenterology and Hepatology, the Netherlands

^j Amsterdam UMC, Location University of Amsterdam, Department of Medical Oncology, Amsterdam, the Netherlands

^k Department of Medical Oncology, Biomedical Research Institute INCLIVA, University of Valencia, Spain

^l Cholangiocarcinoma Foundation, Herriman, Utah, USA

^m Division of Cancer Sciences, The University of Manchester, Manchester, United Kingdom

ⁿ Dept. of Medical Oncology, Clinical Senior Lecturer and Honorary Consultant Medical Oncologist, University of Glasgow and Beatson West of Scotland Cancer Centre, United Kingdom

^o University Medical Center Utrecht Cancer Center, Division of Imaging & Oncology, Utrecht, the Netherlands

ABSTRACT

Introduction: Adjuvant chemotherapy improves survival in patients with resected pancreatic ductal adenocarcinoma (PDAC). The decision to initiate chemotherapy involves both patient and physician factors, decision-specific criteria, and contextual considerations. This study aimed to assess medical oncologists' views on adjuvant chemotherapy following pancreatic resection for PDAC.

Methods: An online survey and case vignette study were distributed to medical oncologists via the Dutch Pancreatic Cancer Group (DPCG), International Hepato-Pancreato-Biliary Association (IHPBA) and related networks.

Results: A total of 91 oncologists from 14 countries participated, 46 % of whom treated more than 40 new PDAC patients annually, with a median experience of 15 years. Significant discrepancies were noted in their recommendations for adjuvant chemotherapy across case vignettes. In patients over 70, 17 % advised against chemotherapy, while 31 % said age was not a factor. Oncologists with less than 10 years of experience and those in non-academic settings were less likely to recommend adjuvant therapy. While 87 % agreed mFOLFIRINOX is the preferred adjuvant treatment, consensus on individual cases was lacking. The recommended

* Corresponding author. Dept. of Surgery, Regional Academic Cancer Center Utrecht, University Medical Center Utrecht Cancer Center & St. Antonius Hospital Nieuwegein, 3508 GA, Utrecht, the Netherlands

E-mail addresses: n.c.biesma-2@umcutrecht.nl (N.C. Biesma), h.van.santvoort@antoniusziekenhuis.nl (H.C. van Santvoort).

* Shared first author.

¹ Shared last author.

<https://doi.org/10.1016/j.ejso.2024.109544>

Received 9 October 2024; Received in revised form 19 November 2024; Accepted 10 December 2024

Available online 12 December 2024

0748-7983/© 2024 The Authors. Published by Elsevier Ltd. This is an open access article under the CC BY license (<http://creativecommons.org/licenses/by/4.0/>).

interval between surgery and chemotherapy ranged from 3 to 26 weeks, with varying reasons for withholding treatment, primarily due to postoperative recovery and performance status.

Conclusions: Our study revealed substantial variation among oncologists in counseling on adjuvant chemotherapy after PDAC resection. This emphasizes the need for more patient involvement in decision-making and improving shared decision-making.

1. Introduction

Pancreatic ductal adenocarcinoma (PDAC) is estimated to become the second leading cause of cancer-related mortality by 2030 [1]. Optimal treatment of PDAC consists of resection of the tumor combined with adjuvant chemotherapy, in patients with early-stage disease. Randomized controlled trials have confirmed the value of adjuvant chemotherapy in resected PDAC [2–10].

Both gemcitabine combination therapy and mFOLFIRINOX (modified fluorouracil, leucovorin, irinotecan, and oxaliplatin) have demonstrated superior oncological survival compared to gemcitabine monotherapy, establishing them as standard adjuvant chemotherapy in current protocols [5,8,9]. However, despite proven benefits, only 54–72 % of patients with resected PDAC receive adjuvant treatment [11–15]. Factors contributing to the shared decision to initiate treatment arise from different domains: decision maker-related criteria (both patient and medical professional specific), decision-specific criteria, and contextual factors [16].

However, since there is little consensus regarding the optimal chemotherapy regimen for adjuvant chemotherapy in PDAC, individual medical oncologists may have considerable impact on the decision-making process. The American Society of Medical Oncology (ASCO) expresses a preference for mFOLFIRINOX [7]. The European Society for Medical Oncology (ESMO) guidelines, state that the optimal type and duration of adjuvant chemotherapy remains unknown [8]. And, although it is recommended to start adjuvant treatment within 12 weeks after pancreatic resection, this 12-week cut off has yet to be investigated as current literature suggests that there is no significant survival benefit in patients who started adjuvant chemotherapy at 6, 8, 9 or 12 weeks postoperatively [4,17,18]. Current guidelines therefore offer medical oncologists considerable room for individual interpretation and a personal approach to shared decision-making. Contextual factors that possibly influence the recommendation include prolonged postoperative recovery, increased age, and low annual surgical center volume of treated patients [11–14]. Also, despite the added value of adjuvant chemotherapy, its toxicity in relation to a relatively low survival benefit remains a matter of concern [5,19,20].

Overall, shared decision-making is known to be influenced by a broad range of parameters and external factors, which differ among medical oncologists and their patients [16,21]. However, the distribution of these factors is unknown and merits further investigation to understand the medical oncologists' role. We therefore performed an international survey study with the aim to evaluate the considerations of medical oncologists when counseling patients to start with adjuvant chemotherapy in resected PDAC.

2. Methods

2.1. Study design

An international expert survey and case vignette study was performed. The questionnaire included 35 general questions and seven case vignettes. The survey period was from November 2022 until November 2023 and the invites were sent out by e-mail. A reminder e-mail was sent four times.

The approached respondents were medical oncologists involved in the management of patients with PDAC and were contacted via the Dutch Pancreatic Cancer Group (DPCG), the International Hepato-Pancreato-Biliary Association (IHPBA), the European-African

Hepatobiliary Pancreatic Association (E-AHPBA), the network of members of the study committee or identified through their contribution to studies on pancreatic cancer. In the invitation, respondents were asked to share the survey with their colleagues specialized in pancreatic cancer. This study was approved by the Scientific Committee of the Dutch Pancreatic Cancer Group (DPCG) [22].

2.2. Decision specific model

To define various factors contributing to the overall decision, the questionnaire of in total 35 questions focused on three different domains (decision maker-related criteria, decision-specific criteria, and contextual factors). The decision-maker related criteria of the medical oncologist included demographics such as age, country of origin, years of experience, and the working environment (academic, non-academic/tertiary referral center, or combination). Additionally, questions were added on the medical oncologist's view on shared decision-making, their own patient experiences in the consultation room and their view on the decision of administering adjuvant treatment and characteristics influencing their decision. Questions from the externally validated '9-item Shared-Decision-Making Questionnaire' were also integrated in our survey in order to provide a comprehensive view upon shared decision making [23]. The case vignettes comprised seven clinical cases, emphasizing on postoperative factors relevant to the overall decision regarding the initiation of adjuvant chemotherapy. The complete survey can be found in the supplementary appendix.

2.3. Statistical analysis

Descriptive statistics were used to analyze demographic characteristics and survey responses. To evaluate which medical professional-related criteria were of influence on their recommendations, respondents were divided in multiple ways based on demographic characteristics (years of experience and working environment). To calculate differences between groups, the Chi-squared test was used for categorical variables and the Mann-Whitney U and Kruskal-Wallis tests were used for continuous variables. Categorical data were presented as counts with proportions. Continuous outcomes were presented as mean with standard deviation or median with interquartile range, as appropriate. P-values of <0.05 were considered to be statistically significant. All analyses were performed using R studio and IBM SPSS Statistics for Windows, version 28.0.0.0 (IBM CORP., Armonk, NY USA).

3. Results

Following the exclusion of duplicates and surveys with empty responses (n = 3), a total of 91 respondents completed the survey and were included in the analysis. Respondents originated from 14 countries, spanning four continents (Table 1, Fig. 1). The median age of the respondents was 45 years (IQR 39–56 years) and 52 respondents (57 %) were male, further medical oncologists' characteristics can be found in Table 1.

3.1. Influence on decision

In total, 40 medical oncologists (44 %) (completely) agreed that they counsel every patient in the same manner, and 31 medical oncologists (34 %) did not (Table 2). Additionally, 33 % of medical oncologists (completely) agreed they do not discuss all available adjuvant

Table 1
Characteristics of 91 participating medical oncologists.

	Total (n = 91)		Total (n = 91)
Country, n (%)	73	Age, median (IQR)	91
The Netherlands	19 [26]		45 (39–56)
United States of America	11 [15]	Sex, n (%)	91
Germany	7 [10]	Male	52 (57)
United Kingdom	6 [8]	Female	37 (41)
Belgium	5 [7]	Prefer not to say	2 [2]
Spain	5 [7]	Experience in years, median (IQR)	89
Italy	5 [7]		15 [7–20]
France	3 [4]	Experience in years, n (%)	91
Ireland	3 [4]	0–5 years	10 [11]
Australia	3 [4]	6–15 years	39 (44)
China	2 [3]	16–25 years	26 [29]
Taiwan	2 [3]	>25 years	14 [16]
Norway	1 [1]	Current work environment, n (%)	91
Israel	1 [1]	Academic hospital	54 (59)
Continent, n (%)	73	Non-academic/tertiary referral center	24 [26]
Europe	54 (74)	Combination	13 [14]
North America	11 [15]	Number of colleagues, median (IQR)	89
Asia	5 [7]		5 [3–15]
Australia	3 [4]	Patients on an annual basis, n (%)	91
		0–20	19 [21]
		21–40	30 (33)
		>40	42 (46)

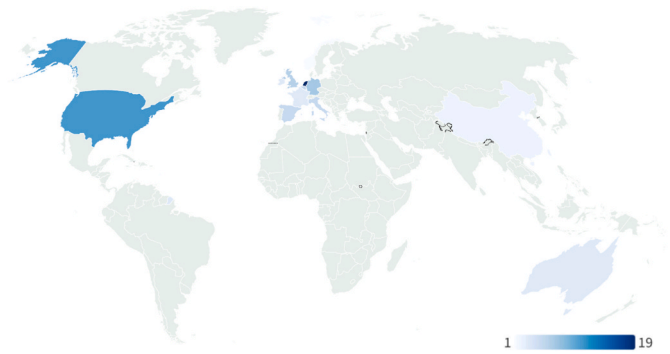


Fig. 1. Number of responding medical oncologists per country.

chemotherapy options and their survival benefits uniformly to every patient.

A significant majority agreed that the postoperative course (97 %), as well as the oncologist’s own opinion on whether the patient can undergo adjuvant chemotherapy (81 %) weigh heavily in the consideration of starting adjuvant chemotherapy. One third of medical oncologists (36 %) felt that the chemotherapy plan they propose is determined before the first consultation, where 35 % disagreed with this statement. Most (87 %) medical oncologists agreed that mFOLFIRINOX is the preferred chemotherapy of choice in the adjuvant setting. When faced with a patient considering refusal of proposed treatment plan, 44 medical oncologists (48 %) agree that they sometimes persuade the patient based on their own judgement, while 24 % disagrees with this practice. Work-environment and work experience did not influence this statement (supplementary table 1, 2 and 3).

Postoperative recovery (76 %) and WHO performance score (66 %) were key criteria taken into consideration by medical oncologists in their decision (Fig. 2). While the criteria social situation (18 %) and resection margin (12 %) were perceived as having the least impact on the decision to recommend adjuvant chemotherapy, 38 medical

Table 2
Survey responses on clinical practice in pancreatic cancer consultation statements.

	Total N = 91
I counsel every patient in the same manner (n, %)	
Completely agree	7 [8]
Agree	33 (36)
Neutral	20 [22]
Disagree	27 (30)
Completely disagree	4 [4]
I explain all systemic therapy options and emphasize the survival benefit in every patient in the same way	
Completely agree	8 [9]
Agree	34 (37)
Neutral	19 [21]
Disagree	29 (32)
Completely disagree	1 [1]
The postoperative course pays a major role in the consideration of starting adjuvant therapy	
Completely agree	30 (33)
Agree	58 (64)
Neutral	2 [2]
Disagree	0
Completely disagree	1 [1]
When I advise a patient to start with systemic therapy, my own opinion on whether or not the patient can undergo therapy weighs heavily	
Completely agree	10 [11]
Agree	64 (70)
Neutral	14 [15]
Disagree	3 [3]
Completely disagree	0
The therapy plan I propose is typically established before the patient walks into the consultation room	
Completely agree	3 [3]
Agree	30 (33)
Neutral	26 [29]
Disagree	26 [29]
Completely disagree	5 [6]
mFOLFIRINOX is the first-choice therapy in the adjuvant setting after pancreatic resection	
Completely agree	41 (45)
Agree	38 (42)
Neutral	8 [9]
Disagree	3 [3]
Completely disagree	1 [1]
If a patient is considering declining systemic therapy, I sometimes persuade him/her based on my own judgment about whether or not to start chemotherapy	
Completely agree	6 [7]
Agree	38 (41)
Neutral	25 [27]
Disagree	21 [23]
Completely disagree	1 [1]

oncologists (42 %) recognized the role of the resection margin (R0/R1) highly in their advice (Table 3). Additionally, 39 medical oncologists (43 %) reported to refrain from recommending adjuvant chemotherapy in cases with an R2 resection margin. The interval between resection and start of adjuvant chemotherapy was acknowledged as a contributing factor, as medical oncologists suggest a maximum interval of 10–12 weeks (IQR) postoperatively, though responses varied widely with intervals from 3 to 26 weeks.

Quality of life emerged as one of the three key criteria taken into consideration in the overall decision of whether or not to advise adjuvant chemotherapy for 22 (24 %) medical oncologists (Fig. 2). Quality of life was primarily assessed through clinical observation (89 %) (Table 3).

3.2. Shared decision-making

All medical oncologists agreed that shared decision-making plays somewhat of a role during the consultation process and the overall decision to start with adjuvant chemotherapy. All statements of the ‘9-item

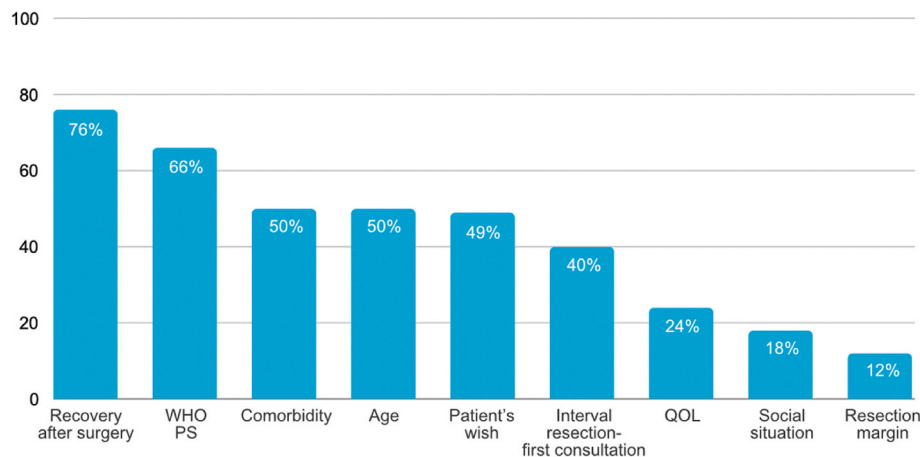


Fig. 2. Key criteria taken into consideration in the overall decision whether or not to advise adjuvant therapy Respondents were asked to select 3 most important criteria, by number and percentage of respondents.

Shared Decision-Making Questionnaire' were agreed upon by the majority of medical oncologists (Supplementary Table 4). Medical oncologists stated that 50 % of the adjuvant chemotherapy plan was reported to be predetermined prior to the first clinical observation (IQR 40–70 %). The influence of the patient's social environment and support system has an importance of 35 % (IQR 20–50 %) on the decision of whether or not to start with adjuvant chemotherapy. The medical oncologist's opinion has an importance of 50 % (IQR 50–80 %) with answers ranging from 0 to 100 %.

3.3. Case vignettes

With exception of one case, opinions on initiating adjuvant chemotherapy for patients with resected PDAC were highly divided (Table 4). There was consensus in case 7, where all 91 medical oncologists (100 %) would initiate adjuvant chemotherapy, with 86 oncologists opting for mFOLFIRINOX (96 %, Fig. 3). Other cases most medical oncologist would advise mFOLFIRINOX, were cases 3 (n = 6, 40 %) and 6 (n = 40, 51 %), involving young patients. The other type of chemotherapy that was proposed by the majority in three cases is gemcitabine combination therapy (cases 1, 2, and 5). Gemcitabine monotherapy prevailed in one case (case 4), with a slightly higher percentage than gemcitabine combination therapy (34 % versus 32 %). This case involved a 75-year-old woman with extensive comorbidities, R2 resection, and general patient hesitance towards adjuvant therapy (see Fig. 4).

In the second and fifth case, age was chosen as one of the reasons not to advise adjuvant chemotherapy by 95 % and 85 % of the medical oncologists, respectively (83- and 86-years old patient, Fig. 3 and Supplementary Table 5). In all cases with postoperative complications (cases 1, 3 and 6), the criterium 'postoperative course' was considered a significant reason not to initiate adjuvant chemotherapy. Social situation emerged as an important reason not to initiate adjuvant chemotherapy in cases 1 (28 %) and 5 (32 %), both involving patients living alone with a Performance Score of 2.

An analysis of medical oncologists with varying years of experience indicated that those with less than ten years of practice were less likely to prescribe adjuvant chemotherapy compared to medical oncologists with ten or more years of experience across all cases, although this did not reach statistical significance (Supplementary Fig. 1).

Medical oncologists practicing in academic centers also exhibited a 17–31 % higher propensity for recommending adjuvant chemotherapy over cases 1–6 compared to colleagues practicing in a non-academic setting, with differences in cases 1, 2 and 4 being statistically significant (52 % vs 21 %, $p = 0.02$; 83 % vs 58 %, $p = 0.03$ and 50 % vs 21 %, $p = 0.02$, respectively). No differences were observed between medical oncologists from academic and non-academic centers in their reasoning.

In other domains, including the interval between resection and start of adjuvant chemotherapy, impact of R2 resection and impact of shared decision-making, there was no difference between oncologists from academic and non-academic medical centers.

4. Discussion

This international expert survey with case vignettes illustrates the intricate shared decision-making process surrounding the initiation of adjuvant chemotherapy in patients with resected PDAC from the medical oncologist's point of view. Considerable inter-rater variability was found among medical oncologists when presented with case vignettes, indicating diverse considerations influencing treatment advice. Factors such as years of experience, interpretation of available evidence and guidelines, country of practice, and the medical oncologist's assessment of the importance of the patient's age, recovery, performance and wishes contribute to these differences. Another important finding of the current study was that medical oncologists consistently emphasized the significance of involving patients in treatment decisions. However, very often (50 %) the medical oncologist's recommendation regarding the initiation of adjuvant chemotherapy was found to be already decided prior to the first consultation with their patient, based on patient characteristics and medical history.

Adjuvant chemotherapy has proven to have added value in patients with resected PDAC in terms of oncological survival [2–10]. Previous studies have shown, however, that only 54–72 % of all patients start with adjuvant chemotherapy [11–15]. Higher age and delayed post-operative recovery were identified as main reasons why patients did not receive adjuvant chemotherapy [9]. Multiple domains in shared decision-making can affect the choice of whether or not to initiate adjuvant chemotherapy. One of which being decision-maker related criteria on both patient and medical professional level. Regarding medical professional-related criteria, work experience and work environment (academic vs non-academic) did have a significant impact on the overall decision to recommend adjuvant chemotherapy. Analysis showed that medical oncologists with more experience and those working in an academic setting were more likely to prescribe adjuvant chemotherapy. This was also reported in a 2015 cross-sectional study which objectified the prescribing habits between academic and non-academic physicians and observed more extensive prescribing patterns in those practicing in academic centers [24].

To further explore the considerations of medical oncologists in a real-world setting, where patients present with unique characteristics, we designed various case vignettes. Of note, the novel guidelines are not adhered to when looking at the responses on the case vignettes. Only cases 6 and 7, which were cases where patients were eligible to receive

Table 3

Survey responses regarding influence on decision to recommend adjuvant chemotherapy.

	Total (n = 91)
From what age do you advise a patient not to proceed with adjuvant therapy, n (%)	
>70 years	15 [17]
>75 years	22 [24]
>80 years	24 [26]
>85 years	2 [2]
Age doesn't play a part in my overall decision	28 (31)
Does the resection margin status (R0/R1) play a part in the overall decision to advise a patient to proceed with adjuvant therapy?	
Yes	38 (42)
Do you recommend adjuvant therapy in the setting of a patient with an R2 resection margin?	
Yes	51 (57)
Up to how many weeks postoperatively do you advise a patient to proceed with adjuvant therapy?	
Median (IQR)	12 [10–12]
0–5 weeks	2 [2]
6–8 weeks	12 [14]
10 weeks	9 [11]
11–12 weeks	48 (56)
13–14 weeks	9 [11]
>15 weeks	6 [7]
How do you evaluate your patient's quality of life before start of systemic therapy?	
By questionnaire	5 [6]
Clinical observation	81 (89)
Other	5 [6]
What percentage of the adjuvant therapy plan is already decided prior to the patient's first consultation with the oncologist postoperatively?	
Median (IQR)	50 % (40–70)
How often, in the last 12 months, has your patient's opinion disagreed with your recommendation regarding the planned course of systemic therapy?^a	
Median (IQR)	2 (0–5)
Never	33 (37)
Rarely	32 (36)
Sometimes	13 [15]
Regularly	8 [9]
Often	1 [1]
I don't know	2 [2]
How often, in the last 12 months, has the therapy plan you proposed deviated from your patient's wishes?^a	
Median (IQR)	0 (0–6)
Never	42 (47)
Rarely	21 [23]
Sometimes	12 [13]
Regularly	9 [10]
Often	4 [4]
I don't know	2 [2]
The patient's social environment and support system plays a role in the decision to start with systemic therapy. How important is this influence in your decision as to whether or not to start with systemic therapy (in percentage)?	
Median (IQR)	35 % (20–50)
In the decision not to start with systemic therapy, how important is your opinion as a medical oncologist in this decision? Please provide an answer on a scale of 0–100 (0 = no influence)	
Median (IQR)	50 % (50–80)

^a There was no uniformity in completing a qualitative or quantitative answer to this question. To calculate the median with IQR, we used all quantitative answers. To calculate the qualitative answers, we used qualitative answers of the medical oncologists (or variations thereof) and converted quantitative answers as follows: Never (0), Rarely [1–5], Sometimes [6–12], Regularly [13–24], Often (>24).

adjuvant mFOLFIRINOX according to the PRODIGE-24 trial, show a uniformity with the current guidelines. These findings affirm the inevitable deviation from guidelines as other variables influence decision-making, highlighting the fragile and unpredictable daily clinical practice for patients with PDAC.

Besides the medical professional related criteria, various decision-specific criteria and contextual factors also influence the decision (not) to initiate adjuvant chemotherapy, with a prolonged recovery after

surgery as biggest component. The timing of adjuvant chemotherapy depends on the postoperative recovery of the patient and is based on few guidelines stating that start of chemotherapy should not exceed 12 weeks post resection [4]. A recent study, investigating the timing of adjuvant chemotherapy in 7548 patients with pancreatic cancer, concluded that shared decision-making between medical oncologists and patients is required in order to individualize when to initiate adjuvant chemotherapy [24]. However, this was not objectified nor analyzed as it was only stated in the key points and no questionnaire, or other measures were used to objectify the impact of shared decision-making [25]. Timing remains a relevant issue, and no survival benefit with different timing was seen in a recent systematic review [17].

Additionally, a study done by Valle et al. showed that completing the intended six chemotherapy cycles was identified as an independent prognostic factor for survival after resection for PDAC, compared to early initiation [18]. Thus, underlining that patients are allowed adequate time for post-operative recovery to maximize the chances of them being fit enough to complete the course. This is also reflected in our study, where a lack of consensus on a strict limit for postoperative timing of adjuvant chemotherapy was observed. The medical oncologists reported a range of 3–26 weeks, possibly because they tailor the timing to the personal situation of the patient.

In an effort to objectify the level of shared decision-making, the Shared Decision-Making Questionnaire-9 (SDM-Q9) was included (Supplementary Table 3). The survey responses did not reflect the results of this questionnaire. Specifically, half of oncologists admitted to having a predetermined treatment recommendation prior to the first consultation, and 46 % agreed they do not explain all systemic treatment options the same way. These findings suggest a need for more comprehensive aiding tools to provide patients with thorough and uniform information to minimize the knowledge gap and maximize the shared decision-making in practice.

Patient age was the third most common factor influencing the decision to refrain from adjuvant chemotherapy, which was most prevalent in the case vignettes. In the survey, 17 % of medical oncologists reported advising patients >70 years against undergoing adjuvant chemotherapy. This is noteworthy, given that randomized trials on adjuvant chemotherapy in PDAC often used higher or no age cut-offs for study eligibility [3,5–7]. Conversely, one out of three medical oncologists stated that age does not play a part in the decision whether to advise adjuvant chemotherapy. This may be because these medical oncologists prioritize the patient's WHO performance status and comorbidities over age, as suggested in Fig. 2, however, this perspective was not reflected in the responses to the case vignettes. This is in line with a recent study that found that postoperative complications did not differ between elderly and younger patients undergoing resection for pancreatic cancer; however, adjuvant chemotherapy was administered less often in elderly patients, possibly leading to a lower survival in this population [12]. Previous studies also open the discussion that factors other than age cutoff alone should be considered when selecting elderly patients for adjuvant treatment [26,27]. For example, both NCCN and ASCO recommend that patients older than 65 years should receive a geriatric functional assessment [7]. Calculating a mortality risk based on a rapid measure of assessing noncancer-related functional loss and comorbidities may provide a more justifiable cutoff point than age alone [26].

The introduction of multi-potent chemotherapy regimens has broadened the choices of adjuvant chemotherapy. The current standard is based upon the outcome of the PRODIGE-24 and the ESPAC-4 trial, where adjuvant gemcitabine monotherapy was found to be inferior regarding overall survival compared to mFOLFIRINOX and gemcitabine plus capecitabine [4,5,8,9]. Our study was set out to determine if this is the case in a non-trial setting. While 87 % of oncologists initially indicated mFOLFIRINOX to be the first-choice chemotherapy, the answers provided in the case vignettes prove that the choice for this chemotherapy is not self-evident. Our results show that mFOLFIRINOX is generally advised to the younger and better-recovered patients,

Table 4
Survey results – case vignettes.

Case vignette	Adjuvant therapy		In case of therapy		Reasons no therapy	
Case 1 Female, 68 years old, 10 weeks post Whipple, R0 resection, T3N1M0 (IIB), complicated postop course, WHO PS 2, widowed, living alone, wish to pursue adjuvant therapy but aware that she has not yet fully recovered	Yes No	49 (43 %) 51 (57 %)	mFOLFIRINOX Gemcitabine combi Gemcitabine mono Other	2 (5 %) 24 (62 %) 10 (26 %) 3 (8 %)	Age Timing Resection margin Postop course WHO PS Social situation Other	2 (4 %) 10 (20 %) 1 (2 %) 34 (68 %) 39 (78 %) 14 (28 %) 4 (8 %)
Case 2 Male, 83 years old, 8 weeks post Whipple, R1 resection, T2N1M0 (IIB), 4 weeks preoperative prehabilitation, WHO PS 1–2, lives with his wife, very motivated towards starting adjuvant therapy	Yes No	69 (77 %) 21 (23 %)	mFOLFIRINOX Gemcitabine combi Gemcitabine mono Other	18 (26 %) 37 (54 %) 12 (17 %) 2 (3 %)	Age Timing Resection margin Postop course WHO PS Social situation Other	20 (95 %) – 3 (14 %) – 6 (29 %) 1 (5 %) 1 (5 %)
Case 3 Male, 61 years old, 12 weeks post Whipple, R0 resection, T1N0M0 (IA), complicated postop course, WHO PS 2, walks with cane, completed 6 cycles of neoadjuvant FOLFIRINOX within study, lives with his wife and works as a goldsmith, hesitant towards adj FOLFIRINOX as it has taken a toll on him	Yes No	15 (17 %) 75 (83 %)	mFOLFIRINOX Gemcitabine combi Gemcitabine mono Other	6 (40 %) 5 (33 %) 2 (13 %) 2 (13 %)	Age Timing Resection margin Postop course WHO PS Social situation Other	1 (1 %) – – 49 (66 %) 32 (43 %) 6 (8 %) 19 (26 %)
Case 4 Female, 75 years old, 6 weeks post distal pancreatectomy, R2 resection, T3N2M0 (III), uncomplicated postop course, WHO PS 1–2, COPD, chronic heart failure and reduced kidney function, lives with her husband, hesitance towards starting adjuvant therapy	Yes No	38 (42 %) 52 (58 %)	mFOLFIRINOX Gemcitabine combi Gemcitabine mono Other	9 (24 %) 12 (32 %) 13 (34 %) 4 (11 %)	Age Timing Resection margin Postop course WHO PS Social situation Other	4 (8 %) – 22 (46 %) 7 (15 %) 33 (69 %) – 28 (58 %)
Case 5 Male, 86 years old, 9 weeks post pancreatic resection, R0 resection, T2N0M0 (IB), uncomplicated postop course, WHO PS 2, permanently disabled due to a boating accident and reliant on a wheelchair, living alone with at home care	Yes No	27 (30 %) 63 (70 %)	mFOLFIRINOX Gemcitabine combi Gemcitabine mono Other	6 (22 %) 13 (48 %) 5 (19 %) 3 (11 %)	Age Timing Resection margin Postop course WHO PS Social situation Other	53 (84 %) – – 1 (2 %) 29 (46 %) 20 (32 %) 3 (5 %)
Case 6 Female, 45 years old, 9 weeks post pancreatic resection, R1 resection, T4N1M0 (III), complicated postop course, WHO PS 1–2, difficulty walking (wheelchair), lives with her husband, active therapy wish but postoperative recovery has taken a toll on her	Yes No	78 (88 %) 11 (12 %)	mFOLFIRINOX Gemcitabine combi Gemcitabine	40 (51 %) 29 (37 %) 4 (5 %)	Age Timing Resection margin Postop course	– – 9 (82 %) –

(continued on next page)

Table 4 (continued)

Case vignette	Adjuvant therapy		In case of therapy		Reasons no therapy	
			mono	%	WHO PS	8 (73
			Other	5 (6	Social	%)
				%)	situation	–
					Other	–
Case 7					Age	–
Female, 57 years old, 6 weeks post distal pancreatectomy, R0 resection, T2N1M0 (IIB),	Yes	90 (100	mFOLFIRINOX	86 (96	Timing	–
uncomplicated postop course, WHO PS 1, history of double mastectomy followed by adjuvant	No	%)	Gemcitabine	%)	Resection	–
therapy (2016), lives alone		0	combi	3 (3	margin	–
			Gemcitabine	%)	Postop course	–
			mono	0	WHO PS	–
			Other	1 (1	Social	–
				%)	situation	–
					Other	–

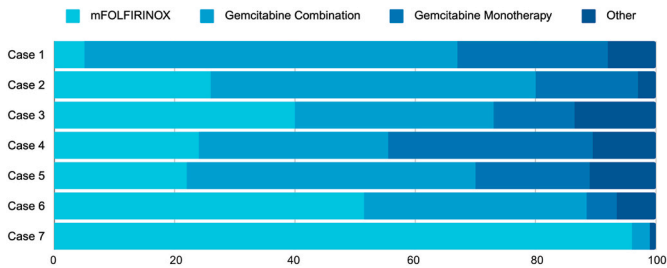


Fig. 3. Preferred adjuvant chemotherapy of medical oncologists with a positive advice towards starting adjuvant chemotherapy per case

The x-axis represents the number of oncologists who chose this option in percentage. Other therapies suggested by the medical oncologists rather than the options given included immune checkpoint inhibitors (PDL1), capecitabine monotherapy, nab-paclitaxel combination, S-1, FOLFIRI and radiotherapy.

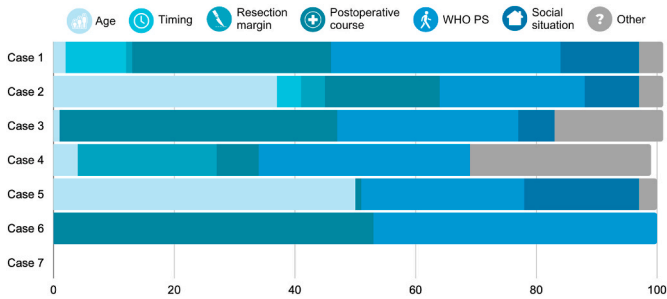


Fig. 4. Main reasons for negative advice towards starting adjuvant chemotherapy per case

The x-axis represents the number of oncologists who chose this reason in percentage. Medical oncologists were allowed to select multiple answers.

Other reasons not to initiate adjuvant therapy suggested by the medical oncologists included comorbidities, balance between (low) benefit of treatment and high likelihood of toxicity-related harm (impact on quality of life), patient hesitancy and pathological tumor status.

reflecting those who meet the selection criteria of phase 3 trials, questioning the applicability of the randomized trials to non-trial setting [5].

The results of this study should be interpreted considering several limitations. First, most medical oncologists originated from Europe, which could minimize the global applicability. Second, as it was possible to provide open answers to the questions, the research group had to interpret some of the results. Third, some questions regarding the same topic were asked repeatedly in different questions with the aim to provoke different viewpoints. As we strived to reach as many international medical oncologists as possible, we have requested various medical oncologists to endorse and distribute our survey to their network. This

resulted in a high applicability to daily practice as we included a relatively large number of medical oncologists who treat at least 40 patients on an annual basis, compared to other studies [28,29].

In conclusion, the decision-making process regarding the initiation of adjuvant chemotherapy in patients with resected PDAC is influenced by multiple factors, including the recommendations of the medical oncologist. This study reveals that medical oncologists employ diverse personal approaches, resulting in a multifaceted impact on shared decision-making. Their recommendations are shaped by their working environment and experience. Future studies on optimal treatment strategies in pancreatic cancer should incorporate the pivotal role of medical oncologists in the decision-making process for (neo)adjuvant chemotherapy. Additionally, investigating the effectiveness of decision-support tools for patients could provide further insight into enhancing shared decision-making.

CRediT author statement

N.C. Biesma, MD, MA1*, M.U.J.E. Graus, MD2* are shared first authors and were responsible for Definition, Conceptualization, Methodology, Software, Validation, Formal analysis, Investigation, Resources, Data Curation, Writing - Original Draft, Writing - Review & Editing, Visualization and Project administration.

All the co-authors (G.A. Cirkel, MD, PhD3, M.G. Besselink, MD, PhD4,5, J.W.B. de Groot, MD, PhD6, B. Groot Koerkamp, MD, PhD7, K. H. Herbschleb MD8, M. Los, MD, PhD8, R.C. Verdonk, MD, PhD9, J.W. Wilmsink, MD, PhD5, 10, A. Cervantes, MD, PhD11, J.W. Valle, MD, PhD,12, L.B.J. Valkenburg-van Iersel MD, PhD2, F.E.M. Froeling, MD, PhD13, I.Q. Molenaar, MD, PhD1, L.A. Daamen, MD, PhD1,14) were responsible for Writing - Review & Editing.

J. de Vos-Geelen, MD, PhD2# and H.C. van Santvoort, MD, PhD1# are shared last authors and were responsible for Conceptualization, Writing-Review&Editing, Supervision, Visualization and Project administration.

Data availability

Data can be requested according to the FAIR principles (Findability, Accessibility, Interoperability, Reproducibility) by contacting the research team.

Funding sources

This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.

Conflict of interest

JdV has served as a consultant for Amgen, AstraZeneca, MSD, Pierre

Fabre, and Servier, and has received institutional research funding from Servier. All outside the submitted work. The other authors have no conflicts.

Acknowledgements

The authors thank the following collaborators for their contribution to the survey:

Appendix A. Supplementary data

Supplementary data to this article can be found online at <https://doi.org/10.1016/j.ejso.2024.109544>.

References

- [1] Siegel RL, Miller KD, Jemal A. Cancer statistics, 2020. *CA Cancer J Clin* 2020;70(1):7–30.
- [2] Katz MH, Wang H, Fleming JB, Sun CC, Hwang RF, Wolff RA, et al. Long-term survival after multidisciplinary management of resected pancreatic adenocarcinoma. *Ann Surg Oncol* 2009;16(4):836–47.
- [3] Klaiher U, Hackert T, Neoptolemos JP. Adjuvant treatment for pancreatic cancer. *Transl Gastroenterol Hepatol* 2019;4:27.
- [4] Specialists FoM. Dutch guideline for the management of pancreatic cancer [Available from: <https://richtlijnendatabase.nl/richtlijn/pancreascarcinoom/startpagina.html>]; 2019.
- [5] Conroy T, Hammel P, Hebbbar M, Ben Abdelghani M, Wei AC, Raoul JL, et al. FOLFIRINOX or gemcitabine as adjuvant therapy for pancreatic cancer. *N Engl J Med* 2018;379(25):2395–406.
- [6] Oettle H, Neuhaus P, Hochhaus A, Hartmann JT, Gellert K, Ridwelski K, et al. Adjuvant chemotherapy with gemcitabine and long-term outcomes among patients with resected pancreatic cancer: the CONKO-001 randomized trial. *JAMA* 2013;310(14):1473–81.
- [7] Khorana AA, McKernin SE, Berlin J, Hong TS, Maitra A, Moravek C, et al. Potentially curable pancreatic adenocarcinoma: ASCO clinical practice guideline update. *J Clin Oncol* 2019;37(23):2082–8.
- [8] Conroy T, Pfeiffer P, Vilgrain V, Lamarca A, Seufferlein T, O'Reilly EM, et al. Pancreatic cancer: ESMO Clinical Practice Guideline for diagnosis, treatment and follow-up. *Ann Oncol* 2023;34(11):987–1002.
- [9] Neoptolemos JP, Palmer DH, Ghaneh P, Psarelli EE, Valle JW, Halloran CM, et al. Comparison of adjuvant gemcitabine and capecitabine with gemcitabine monotherapy in patients with resected pancreatic cancer (ESPAC-4): a multicentre, open-label, randomised, phase 3 trial. *Lancet* 2017;389(10073):1011–24.
- [10] de Jong EJM, Janssen QP, Simons TFA, Besselink MG, Bonsing BA, Bouwense SAW, et al. Real-world evidence of adjuvant gemcitabine plus capecitabine vs gemcitabine monotherapy for pancreatic ductal adenocarcinoma. *Int J Cancer* 2022;150(10):1654–63.
- [11] Mackay TM, Smits FJ, Roos D, Bonsing BA, Bosscha K, Busch OR, et al. The risk of not receiving adjuvant chemotherapy after resection of pancreatic ductal adenocarcinoma: a nationwide analysis. *HPB (Oxford)* 2020;22(2):233–40.
- [12] Henry AC, Schouten TJ, Daamen LA, Walma MS, Noordzij P, Cirkel GA, et al. Short- and long-term outcomes of pancreatic cancer resection in elderly patients: a nationwide analysis. *Ann Surg Oncol* 2022;29(9):6031–42.
- [13] Merkow RP, Bilimoria KY, Tomlinson JS, Paruch JL, Fleming JB, Talamonti MS, et al. Postoperative complications reduce adjuvant chemotherapy use in resectable pancreatic cancer. *Ann Surg* 2014;260(2):372–7.
- [14] Akerberg D, Bjornsson B, Ansari D. Factors influencing receipt of adjuvant chemotherapy after surgery for pancreatic cancer: a two-center retrospective cohort study. *Scand J Gastroenterol* 2017;52(1):56–60.
- [15] Bakens MJ, van der Geest LG, van Putten M, van Laarhoven HW, Creemers GJ, Besselink MG, et al. The use of adjuvant chemotherapy for pancreatic cancer varies widely between hospitals: a nationwide population-based analysis. *Cancer Med* 2016;5(10):2825–31.
- [16] Glatzer M, Panje CM, Siren C, Cihoric N, Putora PM. Decision making criteria in Oncology. *Oncology* 2020;98(6):370–8.
- [17] Sugumar K, Hue JJ, De La Serna S, Rothermel LD, Ocuin LM, Hardacre JM, et al. The importance of time-to-adjuvant treatment on survival with pancreatic cancer: a systematic review and meta-analysis. *Cancer Rep (Hoboken)* 2021;4(5):e1390.
- [18] Valle JW, Palmer D, Jackson R, Cox T, Neoptolemos JP, Ghaneh P, et al. Optimal duration and timing of adjuvant chemotherapy after definitive surgery for ductal adenocarcinoma of the pancreas: ongoing lessons from the ESPAC-3 study. *J Clin Oncol* 2014;32(6):504–12.
- [19] Oettle H, Post S, Neuhaus P, Gellert K, Langrehr J, Ridwelski K, et al. Adjuvant chemotherapy with gemcitabine vs observation in patients undergoing curative-intent resection of pancreatic cancer: a randomized controlled trial. *JAMA* 2007;297(3):267–77.
- [20] Neoptolemos JP, Stocken DD, Bassi C, Ghaneh P, Cunningham D, Goldstein D, et al. Adjuvant chemotherapy with fluorouracil plus folinic acid vs gemcitabine following pancreatic cancer resection: a randomized controlled trial. *JAMA* 2010;304(10):1073–81.
- [21] Beers E, Lee Nilsen M, Johnson JT. The role of patients: shared decision-making. *Otolaryngol Clin North Am* 2017;50(4):689–708.
- [22] Strijker M, Mackay TM, Bonsing BA, Bruno MJ, van Eijck CHJ, de Hingh I, et al. Establishing and coordinating a nationwide multidisciplinary study group: lessons learned by the Dutch pancreatic cancer group. *Ann Surg* 2020;271(4):e102–4.
- [23] Kriston L, Scholl I, Holzel L, Simon D, Loh A, Harter M. The 9-item Shared Decision Making Questionnaire (SDM-Q-9). Development and psychometric properties in a primary care sample. *Patient Educ Counsel* 2010;80(1):94–9.
- [24] Sadigh-Rad L, Majidi L, Javaeiz M, Delirrad M. Comparison of prescribing indicators of academic versus non-academic specialist physicians in Urmia, Iran. *J Res Pharm Pract* 2015;4(2):45–50.
- [25] Ma SJ, Oladeru OT, Miccio JA, Iovoli AJ, Hermann GM, Singh AK. Association of timing of adjuvant therapy with survival in patients with resected stage I to II pancreatic cancer. *JAMA Netw Open* 2019;2(8):e199126.
- [26] Muss HB, Biganzoli L, Sargent DJ, Aapro M. Adjuvant therapy in the elderly: making the right decision. *J Clin Oncol* 2007;25(14):1870–5.
- [27] Dotan E, Catalano P, Lenchik L, Boutin R, Yao X, Marques HS, et al. The GIANT trial (ECOG-ACRIN EA2186) methods paper: a randomized phase II study of gemcitabine and nab-paclitaxel compared with 5-fluorouracil, leucovorin, and liposomal irinotecan in older patients with treatment-naïve metastatic pancreatic cancer - defining a new treatment option for older vulnerable patients. *J Geriatr Oncol* 2023;14(3):101474.
- [28] Augustinus S, van Laarhoven HWM, Cirkel GA, de Groot JWB, Groot Koerkamp B, Macarulla T, et al. Timing of initiation of palliative chemotherapy in asymptomatic patients with metastatic pancreatic cancer: an international expert survey and case-vignette study. *Cancers* 2023;15(23).
- [29] de Rijk FEM, van Veldhuisen CL, Besselink MG, van Hooft JE, van Santvoort HC, van Geenen EJM, et al. Diagnosis and treatment of exocrine pancreatic insufficiency in chronic pancreatitis: an international expert survey and case vignette study. *Pancreatol* 2022;22(4):457–65.