

Patient-reported preferences for oral versus intravenous administration for the treatment of cancer: a review of the literature

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Objective: The emergence of various modes of administration for cancer treatment, including oral administration, brings into focus the importance of patient preference for administration. The purpose of this research was to evaluate the administration preferences of cancer patients, specifically between oral and intravenous (IV) treatment, as well as the factors contributing to preference.

Methods: A literature search was conducted in OvidSP to identify research in which the preferences of cancer patients for oral or IV treatment have been evaluated. Data were analyzed in two stages: 1) those articles that directly compared preference between modes of administration were tallied to determine explicit preference for oral or IV treatment; and 2) all attributes associated with patient preference were documented.

Results: Of the 48 abstracts identified as part of the initial OvidSP search, eight articles were selected for full-text review. One article was removed following full-text review, and seven additional articles were identified through a gray literature search, yielding a total of 14 articles for evaluation. In Stage 1, 13 of the 14 articles compared preference, of which eleven articles (84.6%) reported that patients preferred oral treatment over IV, while two (15.4%) stated that cancer patients preferred IV treatment over oral. In Stage 2, the most frequently reported attributes contributing to preference included convenience, ability to receive treatment at home, treatment schedule, and side effects.

Discussion: Evidence suggests that oncology patients prefer oral treatment to IV. Rationale for preference was due to a number of factors, including convenience, perception of efficacy, and past experience. Further evaluation should be conducted, given the limited data on patient preference in oncology.

Keywords: oncology, patient preference, mode of administration, literature review, mode of administration, oncology, treatment

Introduction

Advances in the detection and treatment of cancer over the last four decades have resulted in growing numbers of cancer survivors in both Europe and the US. It is estimated that the 5-year survival rates for adults have increased up to 50% in both regions.¹ Survivorship can mean complete recovery for a patient in some cases, but in others, patients may experience recurrence, develop another form of cancer, or require intermittent treatment when the disease becomes active, among other trajectories.² An important consideration associated with increased survivorship and continued treatments are the adverse events that can be associated with cancer drugs, which, in turn, negatively affect patients' quality of life. This has led oncologists to focus more closely on the patient's overall treatment experience, taking into account the

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benefits of a therapy as well as its side effects to inform treatment decisions.³

One component of the patient treatment experience is the way in which therapy is administered. Although oral treatment options may not be available in all cancer types or to all patients based on their treatment needs,⁴ the development of cancer drugs that can be administered efficaciously through oral as well as traditional intravenous (IV) methods is becoming increasingly common.^{5,6} In 2014, 40% of the five oncology drugs approved by European Medicines Agency with associated European Public Assessment Reports were orally administered treatments,⁷ indicative of the continued relevance of both IV and oral modes of administration for cancer care.

Scholars have argued that the reduction of the stress and discomfort associated with IV treatments, coupled with the convenience of oral oncology drugs, are benefits of an oral mode of administration.^{8,9} Orally administered cancer drugs are perceived to afford patients greater flexibility than IV treatment, in that the former may allow patients to forgo hospital visits.^{9,10} Research suggests that, when the efficacy and side effects of orally administered cancer treatments are similar to those of IV treatments, patients with incurable malignancies prefer the former, possibly because oral drugs are perceived to afford a greater level of quality of life than their IV counterparts.⁸

However, concerns exist regarding absorption⁸ associated with oral treatments, patient adherence to self-administered medication,^{8,10} and misconceptions regarding their convenience¹⁰ as well as their side effects.¹⁰ Therefore, the most appropriate mode of administration may not be the same in all contexts, but rather is dependent on a patient's needs and preferences. As oncologists become more attuned to patient preferences and their quality of life during treatment, there may be a trend toward prescribing a medication that is most convenient and appropriate for each patient.¹¹

The emergence of various modes of administration, including oral administration, for the treatment of cancer brings into focus the importance of patient preference and the factors that contribute to that preference. The purpose of this paper is to evaluate findings from peer-reviewed literature on patient preference within oncology, and to determine if evidence exists regarding treatment preferences for oral versus IV administration.

Materials and methods

Search strategy

The databases Embase, MEDLINE®, and PsycINFO were searched through the OvidSP platform to identify studies

published from January 2010 through January 2015. The following search terms were used to identify peer-reviewed literature regarding the preferences of patients for oral versus IV administration of cancer treatment: orals or oral by mouth or per os or per oral route or oral route or oral route of drug; intravenous or injection or injecting or intravenous route or intravenous route of drug; preference or prefer or preferred or choice or select or selection; and cancer or oncology or oncology field or oncologies or growth or tumor or malignancy or malignance or melanoma or sarcoma or malignant cells.

The following limitations were set for the search: limit to the English language; limit to human subjects; limit to peer-reviewed journals; and limit to adult subjects.

Finally, reference lists from identified articles were reviewed and a gray literature search was conducted to identify additional articles that may have been missed in the initial search. Gray literature has been defined as materials that may be held by libraries and other institutions but which are not under the control of commercial publishers, or which were not intended to be submitted for publication, such as government reports or conference proceedings.¹² As part of this research, sources meeting this definition as well as published articles identified outside of the databases searched via OvidSP were considered for review.

The gray literature search served as a supplementary search to address any gaps in the OvidSP database search. The gray literature search was conducted by entering similar keywords to those used in the OvidSP database search into an online search engine (Google) and manually screening the hits from the first three pages for sources most relevant to the topic of patient preference for oral versus IV cancer treatment (ie, empirical research directly assessing patient preference for either mode of administration). The limitations outlined earlier were not applied to the gray literature search (ie, non-peer-reviewed sources before January 2010 were considered).

Article selection

The resulting abstracts were uploaded to the Abstrackr (Brown University, Providence, RI, USA) platform for screening. Abstrackr is a software program developed to assist with screening abstracts for systematic reviews, available from: <http://abstrackr.cebm.brown.edu/>. Codes were developed to organize the abstracts into categories to help identify the articles' eligibility for full-text review. For example, abstracts considered for exclusion may have been coded as pediatric population or case study data. Two trained researchers screened and coded all abstracts, and once all citations were screened, they were exported to Microsoft Excel

for an additional level of review. Any discrepancies with respect to eligibility were discussed and resolved. An article was retrieved for full review if the abstract met each of the following criteria: referenced patient-reported preference for oral versus IV administration in a cancer population; derived from a peer-reviewed journal; reported on English-language studies published in the last 5 years; and referenced an adult patient population.

Articles were excluded from full review if the abstract met at least one of the following criteria: concerned patient preference in a pediatric population; focus of article was on case study data; were conference abstracts; or reported on non-patient preference (eg, physician, consensus panels).

Articles that all reviewers agreed upon were retrieved for full-text review, as were relevant articles identified through reference lists and gray literature searches. Following this, some articles were deemed irrelevant after full-text review and excluded from data extraction.

Data analysis

An approach consistent with thematic content analysis informed the review of the selected articles. This allows researchers to provide detailed descriptions of qualitative data to address a targeted research question.¹³ An inductive (“bottom-up”) or deductive (“top-down”) approach can be employed. This analysis relied on a primarily top-down approach in that data most relevant to the research question (ie, patient preference for either mode of administration) were extracted and evaluated; however, the analysis aimed to remain grounded in the data, allowing for concepts deemed important in the literature to be considered, as well (eg, predictors of preference based on prior treatment experience).

Articles selected for full-text review were evaluated using this approach, and salient information pertaining to the study design, sample demographics, therapeutic area, and any notable results was recorded in Table 1. Relevant information relating to patient preference was analyzed in two stages:

1. The first stage consisted of documenting data that reported preference between the two modes of administration (ie, oral treatment versus IV treatment) by patients (eg, the number of patients in a sample stating that they preferred to receive an oral treatment rather than an IV treatment). In this stage, all articles that directly measured preference between modes of administration were reviewed in detail and were tallied to determine how many sources listed explicit preference for oral or IV treatment when the two were compared.

2. The second stage aimed to document all attributes associated with patients’ preferences (eg, what patients liked or disliked about oral or IV treatments regardless of their attitudes toward the alternative mode of administration) identified in the detailed review of each article conducted in the first stage.

Results

Search results

The initial OvidSP literature search identified 48 abstracts as potentially relevant, from which eight articles were selected for full-text review. Following full-text review, one article was removed as failing to meet inclusion criteria. Next, a gray literature search was conducted. The review of abstracts from the OvidSP search demonstrated the need for additional data on patient preference in oncology, specifically additional sources assessing preference in a more diverse oncology patient population, as the majority of the studies focused on, or were predominantly composed of, patients with breast cancer. The gray literature search led to the identification of an additional seven unique sources. These were added to the original seven full-text articles, for a final total of 14 articles.

Article selection

Of the 14 peer-reviewed articles identified for full-text review, eleven^{8,14–23} articles reported patient preference for oral treatment, two articles reported preference for IV treatment,^{6,24} and one article did not explicitly state patient preference for either mode of administration.²⁵ The cancer populations studied in these articles included: breast (n=9), lung (n=3), colorectal (n=4), lymphoma (n=2), other (n=2), bowel (n=1), cholangiocarcinoma (n=1), colon (n=1), gastrointestinal (n=1), genital (n=1), gynecologic (n=1), leukemia (n=1), multiple myeloma (n=1), ovarian (n=3), stomach (n=1), and renal cell (n=1). These conditions are not mutually exclusive, as several studies sampled patients with various cancer types.

Stage 1: preference for oral versus IV mode of administration

Stage 1 of this study evaluated reports of patients’ preference between oral treatments and IV treatments. Of the 14 articles reviewed as part of this study, 13 directly measured patient preference for either mode of administration. Among these, eleven articles (84.6%) reported that patients preferred oral over IV administration and two (15.4%) reported that patients preferred IV over oral administration.

Table 1 provides a summary of results from the articles reviewed. The “study results” column reports Stage 1

Table 1 Data extraction table

Reference, study design	Study sample	Study results/analysis of predictors	Other considerations
Beusterien et al ¹⁴ • Online survey • Conjoint analysis	N=102 adult female patients with breast cancer (any stage) currently receiving neo/adjunct or palliative chemotherapy Age (mean): 54 years, SD=11 Line of chemotherapy: • Adjuvant treatment group (mean): 1.8, SD=0.65 • Palliative treatment group: 2.8, SD=1.3 • Cancer stages: 1 (n=10, 10%), 2 (n=34, 34%), 3 (n=29, 28%), 4 (n=29, 28%)	Support for oral Most preferred mode of administration: 21-day cycle of oral tablets taken twice daily for 2 weeks Least preferred mode of administration: 21-day cycle of 3-hour infusions administered on three separate days Analysis of predictors: none	Toxicity: type and grade of toxicity associated with a treatment was found to be important for driving preference For example, patients were accepting of increased risk of lower grade toxicities (eg, alopecia) when associated with a more convenient mode of administration (oral), but preferred a less convenient regimen if it led to a lower risk of severe toxicities (eg, motor neuropathy)
Borner et al ²³ • Randomized cross-over trial where patients were randomized to either oral or IV chemotherapy for the first treatment cycle, and switched to IV for the second cycle • Oral chemotherapy taken daily for 28 days every 5 weeks. IV chemotherapy administered for 5 days every 4 weeks • Patients completed a Therapy Preference Questionnaire before first treatment cycle and after second treatment cycle	Total N=36 Sample initially randomized to "oral chemotherapy" (n=19): female: n=5, 26.3%; male: n=14, 73.7%; age (median): 58 years (range: 33–73) Prior treatment for malignancy within "oral group": surgery: 18 (95%); radiotherapy: 2 (16%); adjuvant chemotherapy: 6 (32%) Sample initially randomized to "IV chemotherapy" (n=17): female: n=4, 23.5%; male: n=13, 76.5%; age (median): 60 years (range: 39–82) Prior treatment for malignancy within IV group: surgery: 16 (94%); radiotherapy: 2 (12%); adjuvant chemotherapy: 4 (24%)	Support for oral Of the 31 patients who completed the study, 84% (n=26) preferred oral chemotherapy to IV Mean strength of preference for each treatment on a 1–5 scale, where 1=no preference and 5=strong preference, was 4.12 for oral and 3.40 for IV Analysis of predictors: treatment sequence; treatment sequence did not affect whether patients preferred oral or IV treatment. Specifically, after having received both types of treatment, 88% of patients who were randomized to receive oral chemotherapy first preferred oral over IV and of the patients randomized to receive IV treatment first, 79% of patients preferred oral treatment. Therefore, preference for oral over IV chemotherapy was high in both groups	Side effects: prior to undergoing treatment, side effects (specifically risk of infection, vomiting, and diarrhea) were rated as the top three factors associated with treatment preference. After treatment, side effects were rated as the second and third factors, following the ability to receive treatment at home Oral chemotherapy was associated with more diarrhea, but equivalent nausea and vomiting, as compared to the IV treatment, whereas the IV treatment was associated with significantly more stomatitis and hematological toxicity Patients who preferred IV treatment (n=5) had higher incidences of diarrhea, nausea, and vomiting Ability to receive treatment at home: prior to receiving treatment, taking the medication at home was rated as the fourth attribute associated with treatment preference, whereas after completing treatment it was rated first
Calhoun and Roland ²¹ • Survey study	N=39 adult female patients with ovarian cancer who have undergone first-line IV treatment	Support for oral Of the 39 patients surveyed, 56% preferred oral chemotherapy, 28% preferred IV chemotherapy, and 15% did not have a preference Attributes for oral: convenience, efficacy Analysis of predictors: none Support for oral or IV not reported Analysis of predictors: previous treatment experience; patient preference did not vary by number of rounds of chemotherapy Factors most strongly related to treatment preference: survival of 3 months and a 0% risk of fatigue and alopecia	Adherence: forgetting to take medications and/or keep treatment appointments was the most frequently reported reason for treatment non-adherence (n=26, 41.3%) among the 34.8% (n=63) of subjects who had discontinued or were non-adherent to their treatment Toxicity was the second most common reason for treatment non-adherence (n=23, 36.5%)
DiBonaventura et al ²⁵ • Qualitative interviews: cross-sectional survey: choice-based conjoint exercise	N=181 adult female patients with metastatic breast cancer Age (mean): 52 years, SD=9 Ninety percent of patients were currently receiving treatment, most commonly, hormone therapy (47.5%), IV chemotherapy (42%), and oral chemotherapy (24.3%) All patients had previous experience with IV chemotherapy and half (52.5%) had received oral chemotherapy	Support for oral or IV not reported Analysis of predictors: previous treatment experience; patient preference did not vary by number of rounds of chemotherapy Factors most strongly related to treatment preference: survival of 3 months and a 0% risk of fatigue and alopecia	Adherence: forgetting to take medications and/or keep treatment appointments was the most frequently reported reason for treatment non-adherence (n=26, 41.3%) among the 34.8% (n=63) of subjects who had discontinued or were non-adherent to their treatment Toxicity was the second most common reason for treatment non-adherence (n=23, 36.5%)

<p>Fallowfield et al¹⁵</p> <ul style="list-style-type: none"> Qualitative interviews 	<p>N=79 adult female patients with metastatic breast cancer who were newly prescribed oral (n=35) or IV (n=44) bisphosphonate treatment for bone metastases</p> <p>Age (mean): oral: 62, SD=12; IV: 63, SD=13</p>	<p>Support for oral</p> <p>Mean patient satisfaction for treatments: oral =59%; IV =41%</p> <p>Attributes against oral: time required to stand upright, inability to eat or drink</p> <p>Analysis of predictors: none</p>	<p>Dosing schedule: daily for oral, monthly for IV</p> <p>Adherence: 18% (n=6) rarely forgot to take their oral treatment and 21% (n=7) chose to stop taking treatment compared to n=3 who missed an IV treatment</p> <p>Reasons for non-adherence (oral treatment): inconvenience when not at home and the desire to eat or drink before taking the medication</p>
<p>Gornas and Szczyluk¹⁶</p> <ul style="list-style-type: none"> Observational study questionnaire 	<p>N=281 adult female patients with metastatic breast cancer (n=215 completed the preference questionnaire)</p> <p>Age range: 27–77 years</p> <p>Number of lines of prior chemotherapy: 0 (n=38, 17%), first line (n=85, 39%), second line (n=65, 30%), third line (n=22, 10%), fourth line (n=7, 3%), fifth line (n=1, 1%)</p> <p>Number of metastatic sites: 1 (n=57, 26%), 2 (n=92, 42%), 3 (n=55, 25%), 4 (n=14, 6%)</p>	<p>Support for oral</p> <p>Patient preference for oral by line of treatment (1, 2, and 3):</p> <p>Convenience: 52%, 73%, and 72%</p> <p>Ability to stay home during treatment: 65%, 74%, and 56%</p> <p>Attributes for oral: convenience, ability to stay home during treatment, desire to continue working, no contraindications</p> <p>Analysis of predictors: ability to stay at home.</p> <p>Of the 71 patients who provided only one reason for preferring oral to IV treatment, 30 patients (42%) reported the ability to stay home</p> <p>Reason for choosing oral treatment by line of treatment: First line (n=38), convenience (52%); ability to stay home (65%). Second line (n=85), convenience (73%), ability to stay home (74%). Third line (n=95), convenience (72%), ability to stay home (56%)</p>	
<p>Ishitobi et al¹⁷</p> <ul style="list-style-type: none"> Postoperative patients attending follow-up visits at a cancer center were asked to complete a questionnaire regarding their preference between oral and IV treatment 	<p>N=82 postmenopausal adult female patients with early ER+ HER2– breast cancer and who had been previously treated with adjuvant chemotherapy. Patients with evidence of recurrence and those who had previously received neoadjuvant chemotherapy were excluded.</p> <p>Age range: 50–79 years</p> <p>Previous treatment: oral chemotherapy (n=11, 13%), IV chemotherapy (n=71, 87%). No patients had received both treatments</p>	<p>Support for oral</p> <p>Preferred oral to IV 45% versus 35% (20% no preference); all patients who previously received oral treatment preferred oral (n=11, 100%); of the patients who had previously received IV treatment, 41% preferred IV, 37% preferred oral, and 23% had no preference</p> <p>Attributes for oral: place of treatment, anxiety over IV treatment</p> <p>Attributes for IV: treatment duration, efficacy</p> <p>Analysis of predictors: none</p>	<p>Toxicity: dose reduction and/or early cessation of adjuvant chemotherapy as a result of adverse event was not significant between oral (9%) and IV (21%) groups</p> <p>Preference and well-being: patients who received the treatment type they preferred (oral or IV) reported significantly better psychological status (as measured on a 5-point Likert scale, 1= very bad, 5= very good) during chemotherapy compared to those patients who preferred oral treatment and received IV therapy</p> <p>Efficacy: although the treatments were presented as equally effective, patients who preferred IV treatment regarded it to be more effective than oral treatment</p>
<p>Liu et al¹⁸</p> <ul style="list-style-type: none"> Structured survey on medication administration preferences 	<p>N=103 adult patients with incurable cancer likely to receive palliative chemotherapy in the future</p> <p>Female: n=59, 57.3%; Male: n=44, 42.7%</p> <p>Age (mean): 63 years (range: 33–89 years)</p>	<p>Support for oral</p> <p>89.3% preferred oral medication; patients unwilling to stay on oral if IV had higher efficacy</p> <p>Attributes for oral: convenience, problems with</p>	<p>Efficacy: nearly three-quarters of patients were not willing to trade any level of treatment efficacy to receive treatment via their preferred mode of administration (70% unwilling to sacrifice response rate, 74% unwilling</p>

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Table 1 (Continued)

Reference, study design	Study sample	Study results/analysis of predictors	Other considerations
	Primary diagnosis: lymphoma (n=40), breast (n=35), other (n=15), colorectal (n=8), gynecologic (n=8), lung (n=5) Previous treatment: IV chemotherapy (n=41), no chemotherapy experience (n=47), oral chemotherapy (n=9), both oral and IV chemotherapy (n=6)	IV access and needles, environment (can take medication at home), travel, previous IV issues Attributes against oral: forgetting to take oral meds Attributes for IV: someone else can administer, 1-day treatment Differences by demographic factors: no significant differences in preference were found based on previous chemotherapy experience, age, sex, or type of cancer, although differences in attributes associated with preference were found (discussed as follows) Age and sex: women were more worried about IV issues than men, which the authors speculate may be due to having smaller and less accessible veins Convenience was more important to younger men than to any other age cohort, and was significantly more important to younger men than to older women. Convenience was more important to younger men than any other group Support for IV	to sacrifice duration of response) Adherence: four patients stated often forgetting to take their oral medication, and ten patients worried about their adherence Decision-making: patient preference for physician to decide the mode administration (39%), preference for the decision to be made jointly (23%), preference for the patient to make the decision for themselves (38%). Women 65 years and older were 3.5 times more likely to prefer that their physician make this decision than men younger than 65 years (57% versus 15%) All 31 of the 33 patients who listed poor previous experience with IV who preferred oral treatment also listed at least a second reason for their choice. Two of these 31 patients preferred IV regardless of past experience
Mahner et al ⁶ <ul style="list-style-type: none">Patients chose oral or IV treatment at the start of the study. Four patients (4%) did not select their treatment mode of administration prior to the study and were randomized to receive IV (n=3 patients) or oral treatment (n=1 patient)	N=102 adult female patients with platinum-resistant or refractory ovarian cancer Age (median): 72 years (range 65–87) Median number of prior chemotherapy regimens =3 (range: 1–6)	84 patients (82%) selected IV treatment; 14 patients (14%) selected oral Analysis of predictors: none	None
Peeters et al ¹⁸ <ul style="list-style-type: none">Pilot survey regarding oncology patients' preferences for maintenance therapiesPreference was assessed at start of chemotherapy (T0), after two cycles (T1), and after four cycles (T2)	N=30 adult patients with stage 5 non-small cell lung cancer scheduled to begin first-line platinum-based doublet chemotherapy Female: n=13, 43.3%, male: n=17, 57.0%; age (median): 66 (range: 32–79) Disease control was achieved in 60% of patients after four cycles of chemotherapy	Support for oral Both oral and IV were acceptable; 90% preferred oral; IV acceptability increased with additional courses of chemo Attributes for IV: experience with IV Analysis of predictors: efficacy; patients appear to favor MT as long as survival expectations are several months (83%, 67%, and 43% of patients agreed MT was worthwhile when associated with survival of	Side effects: three-quarters of patients stated they would tolerate mild or moderate toxicity with MT The authors argue that prolonged symptom control is important to non-small cell lung cancer patients given that less than one-fifth would choose a treatment associated with a survival of 3 months, but almost 70% stated they would opt for a treatment that improved their quality of life even without survival benefit

<p>6, 3, or 1 months, although support decreased with additional lines of chemotherapy)</p> <p>Symptom relief: similarly, support for symptom relief and tumor control (with no associated survival benefit) were important to patients (eg, about 90% of patients at T0), but this decreased with additional lines of chemotherapy</p> <p>Support for IV</p> <p>Of the 49 patients evaluated that completed the study, 30 (61%) preferred IV chemotherapy and opted to receive this mode of administration for an additional 12 weeks, whereas oral chemotherapy was preferred and continued by 19 (39%) patients</p> <p>Following 12 weeks of additional treatment with the mode of administration selected by the patients, four patients stated that they would have preferred to receive the other mode, specifically, n=3 would have chosen oral and n=1 would have chosen IV</p> <p>Median strength of preference was rated high for both modes of administration (grade 4 or 5)</p> <p>Attributes for IV: side effects (less diarrhea, nausea, tiredness); less interference with daily activities</p> <p>Attributes for oral: preference for pills; preference for taking medication at home</p> <p>Analysis of predictors: treatment sequence; a greater percentage (46%) of patients who were randomized to receive oral treatment first preferred oral treatment over IV, whereas 30% of patients treated with IV first preferred oral treatment</p> <p>Support for oral</p> <p>If given the choice between two equally effective oral or IV chemotherapy treatments, 89.3% of women treated with oral chemotherapy would choose this treatment again compared to 67.1% of patients treated with IV chemotherapy</p> <p>Attributes for oral: personal benefit; less impact on daily/family life; easier to cope with disease; autonomy; less side effects</p> <p>Attributes against IV: everyday life affected by</p>	<p>N=60 adult patients with histologically proven adenocarcinoma of the colon or rectum</p> <p>Sample initially randomized to oral chemotherapy: female: n=14 (46.7%); male: n=16 (53.3%); age (median): 63 years (range: 45–79 years); adjuvant therapy: 26 (86.7%); palliative therapy: 4 (13.3%)</p> <p>Sample initially randomized to IV chemotherapy: female: n=15 (50.0%); male: n=15 (50.0%); age (median): 69 years (range: 36–81 years); adjuvant therapy: 27 (90.0%); palliative therapy: 3 (10.0%)</p>	<p>Pfeiffer et al²⁴</p> <ul style="list-style-type: none"> Patients were randomized to either oral or IV treatment, then crossed over to the alternative mode of administration. After receiving both modes of administrations patients selected one mode to receive for an additional 12 weeks of treatment The Therapy Preference Questionnaire developed by Borner et al⁸ was administered to patients prior to the start of treatment, after completing treatment with both modes of administration, and after selecting a treatment to receive for 12 additional weeks 	<p>Side effects: side effects were ranked as the top three factors associated with preference prior to treatment, specifically risk of infection, vomiting, and diarrhea</p> <p>In the group of patients receiving IV then oral treatment, two cases of grade 3 toxicity were reported with IV treatment compared to eleven cases with oral. As oral treatment was associated with greater side effects and preferred less by patients than IV, the authors concluded that side effects are more important to patients' treatment preferences than location of treatment administration (home or hospital)</p> <p>Perceptions of oral chemotherapy: most of the overall sample (50% or more of patients receiving both oral and IV chemotherapy) reported strongly agreeing or agreeing with the following:</p> <ul style="list-style-type: none"> There is a personal benefit to receiving oral versus IV chemotherapy Everyday life is affected by hospital trips in order to receive IV chemotherapy Oral chemotherapy affects daily life/family less than IV chemotherapy
<p>Schott et al²²</p> <ul style="list-style-type: none"> Survey of treatment preferences for patients currently receiving oral or IV chemotherapy 	<p>N=224 adult female patients with histologically confirmed breast cancer currently receiving IV or oral chemotherapy</p> <p>Sample receiving oral chemotherapy (n=60): age (mean): 55.8 (range: 26–81)</p> <p>Current treatment: neoadjuvant: 0; adjuvant: 0; palliative: 60 (100%)</p> <p>Prior experience with oral chemotherapy: 12 (20%)</p> <p>Sample receiving IV chemotherapy (n=164): age (mean): 52.6 (range: 30–76)</p> <p>Current treatment: neoadjuvant: 10 (6.1%); adjuvant: 95</p>		

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Table 1 (Continued)

Reference, study design	Study sample	Study results/analysis of predictors	Other considerations
	(57.9%); palliative: 59 (36.0) Prior experience with oral chemotherapy: 20 (12.2%)	<p>hospital visits to receive treatment</p> <p>Mode of administration received: significantly more patients receiving oral treatment compared to patients receiving IV treatment reported agreement with following statements regarding oral mode of administration:</p> <p>It provides personal benefit to the patient</p> <p>It has less impact on patients' daily life and families</p> <p>It makes it easier to cope with disease</p> <p>It makes it easier to handle one's disease by providing patients with more autonomy administration</p> <p>It makes patients feel less ill than IV treatment</p> <p>It has less side effects than IV treatment</p> <p>It is as effective as IV chemotherapy</p> <p>There were no significant differences between oral and IV-treated patients in terms of their fear of taking oral medication incorrectly, and no significant differences based on age (50 years and older versus younger than 50 years)</p> <p>Moderately strong significant correlations were identified amongst several survey questions, the strongest being the correlation between strongly agreeing that oral chemotherapy could help patients to better cope with their disease and the belief that oral chemotherapy provides patients with more autonomy</p>	<ul style="list-style-type: none"> Oral chemotherapy makes it easier to handle one's disease by providing patients with more autonomy outside of the clinic Oral chemotherapy is as effective as IV <p>Overall, most patients did not believe that an oral chemotherapy treatment would make it easier to cope with their disease; that it would make them less ill or have less side effects than IV treatment; and did not report fear of taking oral medication incorrectly</p>
Seaman et al ¹⁹	<p>N=14 adult patients with active advanced cancer receiving LMWH for at least three consecutive months to treat venous thromboembolism</p> <p>Female: n=8 (57.1%); male: n=6 (43.0%); age (mean): 66 (range: 52–84)</p> <p>Primary cancer type: breast (n=3), ovarian (n=3), colorectal (n=2), bowel (n=1), cholangiocarcinoma (n=1), colon (n=1), lung (n=1), renal cell (n=1), stomach (n=1)</p> <p>Sites of metastases (not mutually exclusive): bone (n=3), cervical nodes (n=1), liver (n=2), lung (n=2), lymph nodes (n=2), mesenteric nodes (n=1), soft tissue metastases (n=1)</p> <p>Stage: IV (n=10), IIIC (n=2), locally advanced with lymph node involvement (n=1), unknown (n=1)</p>	<p>Support for oral</p> <p>Majority of patients hypothetically preferred oral treatment; all valued efficacy over convenience and reported daily IV treatment was an acceptable "necessary evil"</p> <p>Attributes for IV: ability to treat illness</p> <p>Attributes against IV: side effects</p> <p>Analysis of predictors: none</p>	<p>Efficacy: patients preferred a more effective injection over a more convenient oral medication</p> <p>Adherence: only one participant reported missing a dose of LMWH</p>

Teuffel et al ²⁰	Support for oral	None
<ul style="list-style-type: none"> • Patient interviews assessing mode of administration (oral versus IV) preference in four hypothetical settings 	<p>N=78 adult patients with FN receiving treatment for cancer</p> <p>Female: n=46 (59.0%); male: n=32 (41.0%); age (mean): 54 (range: 20–88)</p> <p>Cancer type: genital (n=21, 26.9%), gastrointestinal (n=17, 21.8%), leukemia (n=14, 17.9%), lymphoma (n=7, 9.0%), breast (n=7, 9.0%), other (n=6, 7.7%), multiple myeloma (n=3, 3.8%), lung (n=3, 3.8%)</p>	<p>75% preferred an outpatient setting; 36% of patients preferred oral administration, and 21% preferred IV administration</p> <p>Analysis of predictors: differences by demographic factors: demographic (age, sex, marital status, education level, employment status, health benefit plan, income, travel time to hospital) and disease-specific factors (history of FN; diagnosis of leukemia, lymphoma, or myeloma; relapsed disease; quality of life) were not significantly related to treatment preference</p>
<p>Abbreviations: IV, intravenous; SD, standard deviation; ER+, estrogen receptor-positive; HER2–, human epidermal growth factor receptor 2-negative; LMWH, low-molecular-weight heparin; FN, febrile neutropenia; MT, maintenance therapy.</p>		

and Stage 2 results and includes findings on patients' preferences for mode of administration, details reported by the sample population, quantitative results, and attributes associated with preference.

Amongst the studies reviewed, six included patients with breast cancer only and an additional three articles included patients with breast cancer, among other cancers. Two articles studied patients with colorectal cancer only. With the exception of four studies, most include a large sample size of >50 patients. Seven studies stratified findings by predictors, such as previous treatment experience, age, and sex.

While there was a clear trend depicting patient preference for oral versus IV treatment, some findings were inconclusive across studies. Both Borner et al²³ and Pfeiffer et al²⁴ studied patient preference using the Treatment Preference Questionnaire in colorectal cancer using a similar study design (a crossover study where patients were first treated with either oral or IV chemotherapy then with the other mode of administration). Borner et al reported that patients preferred oral chemotherapy over IV, whereas Pfeiffer et al reported that patients preferred IV over oral. Pfeiffer et al attributed this to the fact that more side effects were experienced with oral capecitabine than the intravenous Nordic fluorouracil/leucovorin taken by patients in their sample, leading patients to prefer reduced toxicity over convenience.

Some studies reported differences in treatment preference or perceptions of treatment by demographics, such as age. For example, Liu et al⁸ reported that convenience was more important to younger male patients than older female patients, whereas other studies did not find significant differences when evaluating results by age. Specifically, Schott et al²² compared views on oral and IV treatment by age in a German breast cancer population. The authors reported that there were no significant differences between older (those over the age of 50 years) and younger patients in terms of their views on how daily life is impacted due to hospital visits for IV treatment, and no differences in terms of level of concern about taking oral medication incorrectly. That is, both age groups reported that IV treatment had a medium-to-strong impact on daily life and neither group was worried about taking oral treatments incorrectly.

Stage 2: attributes associated with patient preference

This section reports all attributes identified in the published literature that were associated with patients' mode of administration preferences.

Twelve of the 14 articles reported attributes associated with patient preference. Among the articles evaluating

Table 2 Positive attributes associated with oral administration reported by patients with cancer

Attribute	Description of attribute	Study sample
Able to take at home ^{8,16,24}	Ability to receive treatment at home	Patients with metastatic breast cancer; ¹⁶ patients with a primary diagnosis of lymphoma, breast, colorectal, gynecologic, lung, or other cancer; ⁸ patients with colorectal cancer ²⁴
Convenience ^{8,16,21}	Treatment regarded as a more convenient way of taking medication	Patients with metastatic breast cancer; ¹⁶ patients with a primary diagnosis of lymphoma, breast, colorectal, gynecologic, lung, or other cancer; ⁸ patients with ovarian cancer ²¹
Desire to continue working ¹⁶	Desire to continue one's job during treatment	Patients with metastatic breast cancer
No contraindications ¹⁶	The lack of contraindications associated with IV or combined treatment	Patients with metastatic breast cancer
Previous issues with IV treatment ⁸	Description of attribute not reported	Patients with a primary diagnosis of lymphoma, breast, colorectal, gynecologic, lung, or other cancer
Problems with IV access and needles ⁸	Issues such as "pain and difficulty starting an IV line"	Patients with a primary diagnosis of lymphoma, breast, colorectal, gynecologic, lung, or other cancer
Travel ⁸	Description of attribute not reported	Patients with a primary diagnosis of lymphoma, breast, colorectal, gynecologic, lung, or other cancer
Place of treatment ¹⁷	Description of attribute not reported	Postmenopausal patients with early ER+/HER2- breast cancer
Efficacy ²¹	Perception that oral mode of administration for treatment was efficacious	Patients with ovarian cancer
Personal benefit ²²	Description of attribute not reported	Patients with breast cancer
Impact on daily life and relationships ²²	Oral chemotherapy has less of impact on one's daily life and family than IV treatment	Patients with breast cancer
Coping ²²	Oral chemotherapy makes it easier to cope with one's disease	Patients with breast cancer
Autonomy ²²	Oral chemotherapy makes it easier to handle the disease by providing patients with more autonomy outside the clinic	Patients with breast cancer
Side effects ²²	Oral chemotherapy perceived to have fewer side effects and to make patients less ill compared to IV treatment	Patients with breast cancer
Mode of administration ²⁴	Preference for treatment in pill form	Patients with colorectal cancer

Abbreviations: IV, intravenous; ER+, estrogen receptor-positive; HER2-, human epidermal growth factor receptor 2-negative.

preference, "convenience"^{8,16,21} and ability to receive treatment at home^{8,16} were the most frequently reported reasons for preferring an oral mode of administration. Time required to stand upright (specifically, the need to remain standing for 30 minutes after taking oral bisphosphonate treatment),¹⁵ the inability to eat or drink,¹⁵ and forgetfulness⁸ were the only negative aspects of oral treatments reported by patients.

The most frequently reported rationale for patient preference for IV treatment among cancer patients included concepts related to treatment schedule, specifically "completion of treatment in 1 day",⁸ and "treatment duration".¹⁷ Side effects¹⁹ and impact on daily life²² were the only negative aspects of IV treatment reported in the reviewed articles.

Three articles^{23–25} provide patient preference attributes, but did not directly relate them to either oral or IV modes of administration. The attributes included the following: the treatment does not lead to side effects (infection, vomiting, diarrhea, painful mouth sores, nausea, tiredness),^{23,24} can be

taken at home,^{23,24} is a pill,^{23,24} does not affect mood or daily activities,^{23,24} is taken at hospital,^{23,24} is an injection,²⁴ does not cause pain,²⁴ cancer got better,²³ others (family, friends) preferred the treatment,²³ efficacy,²⁵ side effects,²⁵ cost,²⁵ and dosing regimen.²⁵

Tables 2–5 provide a description of the positive and negative attributes associated with oral and IV modes of administration as reported by cancer patients.

Discussion

The results of this literature review suggest that, in patients with cancer, a preference for oral treatment administration over IV has been reported. In this selected sample of studies, convenience and ability to receive treatment at home were the most frequently reported factors associated with patient preference for oral treatment, possibly relating to the fact that oral treatments may allow patients to forgo or reduce the number of hospital visits in comparison to IV treatment.¹⁰ In those

Table 3 Negative attributes associated with oral administration reported by patients with cancer

Attribute	Description of attribute	Study sample
Time required to stand upright ¹⁵	Refers to oral bisphosphonate treatment, where patients must remain upright for at least 30 minutes to limit epigastric pain	Patients with metastatic breast cancer being treated for bone metastases with bisphosphonates
Inability to eat or drink ¹⁵	Refers to oral bisphosphonate treatment, which must be taken in the morning on an empty stomach; patients reporting wanting to drink or eat beforehand as a reason for non-adherence	Patients with metastatic breast cancer being treated for bone metastases with bisphosphonates
Forgetfulness ⁸	Easy to forget to take oral medication	Patients with a primary diagnosis of lymphoma, breast, colorectal, gynecologic, lung, or other cancer

studies where preference was reported for IV administration, the treatment schedule, specifically treatment duration, was the most frequently reported factor regarded as a positive attribute associated with receiving IV treatment.

It is important to note that while cancer patients in these studies preferred oral over IV treatment, it was also reported that patients were generally unwilling to accept reduced efficacy^{8,19} or greater treatment toxicity²⁴ in favor of other treatment attributes, such as convenience. However, when patients rated efficacy as less important than other treatment factors such as convenience, researchers speculated that this was because patients were made aware that the oral and IV formulations were equally effective.²³ Therefore, patients' assessments about the efficacy and toxicity of a treatment, whether known or perceived, appear to continue to drive preference for mode of administration over other potential personal benefits that a patient may value.

Additionally, there was some evidence in the literature reviewed that treatment preferences for mode of administration may relate to factors such as line of treatment or demographic characteristics. For instance, one article reported that the percentage of breast cancer patients who

cited convenience as a reason for choosing oral treatment increased by 20 percentage points between the first compared to second and third lines of treatment, from 52% to 73% and 72%, respectively.¹⁶ Another study reported that convenience was a more important treatment attribute to younger men than women or patients in other age groups, and that women were more likely to report that starting an IV line was a painful and/or difficult experience.⁸

Scholars have noted that patients' treatment experiences and preferences are more salient than ever for two reasons: not only are cancer patients living longer due to improved cancer therapies, but their treatments are also often associated with similar survival benefits.³ Therefore, patients are receiving medical care for longer and are able to choose between therapies that may be associated with different degrees of side effects and/or impacts to their functional ability. Therefore, clinicians have been prompted to evaluate how treatments affect patients' outcomes both in terms of disease control and quality of life.

Research also suggests that experts may not value oral cancer treatments as strongly as their patients do, and that they have concerns about its appropriate administration. A survey of 400 oncologists found that while the

Table 4 Positive attributes associated with IV administration reported by patients with cancer

Attribute	Description of attribute	Study sample
Efficacy ⁸	Perception that IV treatment is more effective than oral	Patients with a primary diagnosis of lymphoma, breast, colorectal, gynecologic, lung, or other cancer
Someone else can administer ⁸	Preference for treatment that one does not have to worry about administering to oneself	Patients with a primary diagnosis of lymphoma, breast, colorectal, gynecologic, lung, or other cancer
Experience with IV ¹⁸	Refers to greater acceptance of IV treatment after previously undergoing chemotherapy	Patients with stage 5 non-small cell lung cancer
Ability to treat illness ¹⁹	Perception that IV treatment helped to keep one's disease under control	Patients with cancer-associated venous thromboembolism, with the following primary cancer type: breast, ovarian, colorectal, bowel, cholangiocarcinoma, colon, lung, renal cell, and stomach
Treatment schedule ^{8,17}	Preference for treatment that can be administered in 1 day or for a shorter duration of time	Postmenopausal patients with early ER+/HER2- breast cancer and who had been previously treated with adjuvant chemotherapy; ¹⁷ patients with a primary diagnosis of lymphoma, breast, colorectal, gynecologic, lung, or other cancer ⁸
Interference with daily activities ²⁴	Perception that IV treatment interferes less with one's daily life	Patients with colorectal cancer

Abbreviations: IV, intravenous; ER+, estrogen receptor-positive; HER2-, human epidermal growth factor receptor 2-negative.

Table 5 Negative attributes associated with IV administration reported by patients with cancer

Attribute	Description of attribute	Study sample
Side effects ^{19,24}	Patients reported side effects associated with treatment that impacted their daily lives (eg, severe shortness of breath, diarrhea, vomiting, tiredness)	Patients with stage 5 non-small cell lung cancer; ¹⁹ patients with colorectal cancer ²⁴
Impact on daily life ²²	Everyday life affected by hospital visits to receive IV treatment	Patients with breast cancer

Abbreviation: IV, intravenous.

most commonly reported recommendation for a first-line, single-agent therapy for the treatment of metastatic colorectal was oral therapy (42%), twice as many oncologists reported that their patients would prefer this mode of administration. Just 8% of clinicians reported that their patients would prefer IV treatment over oral treatment alternatives. While most oncologists (77%) reported that patients and their clinicians should make treatment decisions jointly, 16% felt that clinicians alone should make the decision. Main reasons for not prescribing oral chemotherapy included issues surrounding efficacy, compliance, income, and side effects. Therefore, both clinicians and patients alike recognize the advantages and disadvantages associated with oral and IV modes of administration, although patients appear to support the use of oral chemotherapy more so than their clinicians.

Studies regarding patient preference in other disease areas, such as schizophrenia and diabetes, have reported that IV administration is preferred over oral treatments, suggesting that the findings produced in studies of cancer patients may not be applicable to other conditions. For example, Caroli et al reported that patients with schizophrenia preferred IV to oral treatment, for reasons such as the treatment schedule, perceived efficacy, and the decreased risk of forgetting to take the treatment, despite the fact that some patients reported disliking injections. Schizophrenia preference attributes were characterized by nonadherence to oral medications and the refusal of some patients to take the medications at home, issues that may not be experienced by oncology patients.²⁶ A further example from Casciano et al suggests that prior experience with IV treatment relates to greater acceptance of this mode of administration for type 2 diabetes patients, a condition associated with arguably greater exposure to IV treatment than cancer.²⁷

There are some limitations to this study. First, the search terms and limitations may have prevented identification of articles addressing the substantive topics (eg, articles in non-English journals). Second, the predominance of articles that included breast cancer populations (nine of the 14 reviewed articles) may hinder the ability to extrapolate the findings reported in this paper to other cancer types. Additionally, the exclusive focus on the peer-reviewed literature may provide a limited understanding regarding how treatment

choices are made by patients outside of hypothetical and/or clinical trial study contexts, and of their perceptions of these modes of administration in a real-world setting. Referring to patient blogs and personal accounts on social media, data from patient and/or expert interviews, and other sources that rely on open-ended or spontaneous methods to elicit patients' actual experience with different modes of administration for oncology treatment would supplement findings from the literature. Lastly, it should be reiterated that not all cancer patients may have the opportunity to choose between orally or intravenously administered treatment for their disease, for various reasons such as oral formulations not being available in their indication⁴ or needing to receive both IV as well as oral treatment rather than being able to choose between the two.

The conclusions presented in this paper were drawn from a small sample of articles that included a wide range of cancer types and possible treatment regimens. Patient preference may vary by cancer type and treatment offerings, which warrants future research that assesses preference in one cancer type in a larger patient sample, ideally in a population other than breast cancer, as breast cancer appears to have been the focus of much of the literature on mode of administration preference thus far. The findings from this review can serve as the foundation for understanding attributes that may relate to oncology patients' treatment preferences and can inform measurement of patient preference in a larger empirical study.

Despite these limitations, this review provides several important conclusions and avenues for further research. The results from recent clinical trials in ovarian cancer have pointed to the importance of personalized treatment plans for patients depending on their type and stage of disease, demonstrating the importance of conducting research aimed at better understanding preference for different modes of administration.²⁸ However, the majority of articles reviewed as part of this study did not thoroughly evaluate preference by line of treatment or stage of disease, both of which may be associated with valuing certain aspects of a treatment over others.

In conclusion, among the articles reviewed, support was found to suggest that cancer patients prefer oral over IV treatment. Preference for a mode of administration can be associated with numerous factors, including convenience, perception of efficacy, and past treatment experience. However, as caveated

earlier, further research is needed to determine whether this holds true in cancer patient populations other than breast cancer. Although prior research may have broadly addressed the factors associated with treatment that are of importance to cancer patients, a targeted evaluation of how these relate to preference for oral versus IV treatment is needed.

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