Supportive Care in Cancer (2019) 27:3179–3182
https://doi.org/10.1007/s00520-019-04863-5

COMMENTARY

Oxaliplatin-desensitization procedure is safe and feasible in an outpatient cancer unit in France

Damien Botsen[1,2] · Elise Lepoix[1] · Camille Mazza[1] · Mathilde Brasseur[1,2] · Anne Grange[3] · Florian Slimano[1,4] · Olivier Bouché[1,2]

Received: 26 September 2018 / Accepted: 9 May 2019 / Published online: 17 May 2019

Abstract

This study was undertaken to assess the previously unevaluated safety and feasibility of oxaliplatin-desensitization procedure add a French ambulatory cancer unit, which is a current topic in oncology. Our findings demonstrated that oxaliplatin-desensitization was safe and feasible in our ambulatory cancer unit. In routine practice, all these procedures are done on an inpatient basis starting at least the day before. Those results could change oncological practices in France and improve patients' quality of life and lower costs associated with inpatient administration.

Keywords Desensitization procedure · Safety · Ambulatory · Anticancer drugs

Commentary

Oxaliplatin-based regimens have dramatically improved the treatment of gastrointestinal cancers but oxaliplatin-induced hypersensitivity reactions (HSRs) are unpredictable and can lead to permanent treatment discontinuation. Reported frequencies ranged from 10% to 25% [1, 2] and their most severe form, anaphylaxis, occurred in 0.5% of oxaliplatin-treated patients [3]. HSRs usually occur after multiple infusions, suggesting an immediate type-I HSR. Skin-prick tests have been used to predict hypersensitivity to platin-based drugs, which induce IgE-mediated reactions, with a high negative-predictive value [4]. Skin tests should be done preferably at least 2 weeks after HSRs [4], even though no standard practice is currently recommended.

Because they are time-consuming and complex [2], desensitization protocols are rarely used in routine practice. In France, all those procedures have routinely been administered on an inpatient basis, with the patient staying overnight [5, 6]. Desensitization-protocol safety is well-known [2] and this procedure has been evaluated in an ambulatory setting in the USA, where it is frequently used. However, feasibility in the outpatient setting in France has not yet been established and it could improve patients' quality of life and lower costs associated with inpatient administration. This study was undertaken to assess the safety and feasibility of an oxaliplatin-desensitization procedure in an outpatient cancer unit in France.

The patient cohort of our outpatient cancer unit (UMA-CH) in a French teaching hospital was retrospectively analyzed. We reviewed the medical charts all patients treated with an oxaliplatin-desensitization regimen in our unit. Premedication consisted of an oral

✉ Damien Botsen
damien.botsen@gmail.com

[1] Ambulatory Cancer Unit, CHU Reims, Robert-Debré Hospital, Avenue rue du Général Koenig, 51092 Reims Cedex, France

[2] Department of Gastroenterology and Digestive Oncology, Reims University Hospital, Reims, France

[3] Department of Immunoallergy and Dermatology, CHU Reims, Robert-Debré Hospital, Avenue General Koenig, Reims, France

[4] Department of Pharmacy, CHU Reims, Robert-Debré Hospital, Avenue General Koenig, Reims, France

administration of antihistaminergic (dexchlorpheniramine Polaramine® 2 mg) taken 48 and 24 h and 30 min before, and the intravenous infusion of corticosteroids (methylprednisolone Solumedrol® 120 mg) administered 2.5 h prior to starting the process, regardless of skin-test results and without any stratification. Oxaliplatin was solubilized in a single bag and administration was started at a slower infusion rate (thereby delivering a lower oxaliplatin concentration) that was gradually increased over time for a total of 6 h (Table 1). Patients had to undergo at least two desensitization protocols before being retreated with a conventional oxaliplatin-based regimen over 6 h at a fixed infusion rate. HSRs were classified from grade 1 (transient rash, fever < 38 °C) to grade 4 (anaphylaxis), according to National Cancer Institute Common Terminology Criteria for Adverse Events v4.0 [7]. Outpatient safety was managed according to our current practices, as follows: the oxaliplatin infusion is stopped, corticosteroids are administered, oxygen therapy and rapid intensive care unit (ICU) admission, if necessary. Demographic data, number of infusions before HSR, HSR description, skin-test results, and desensitization procedures were obtained from patients' charts and analyzed (Table 2).

Between January 2016 and July 2018, among 431 patients treated with oxaliplatin, 24 (5.6%) experienced HSRs.

Seven patients (4 men, median [range] age 61 [33–83)] years), five with esophageal or gastric and two with colorectal cancers were consecutively enrolled for desensitization once the procedure became available. A median [range] of 5 [2–7] infusions were administered before HSRs that were grade 3 ($n = 1$) or less ($n = 6$). Among the six patients who underwent skin testing at least 2 weeks after HSRs, three were positive. Sixteen desensitization-protocol infusions were given in our unit. All patients were compliant with premedication taken at home 48 and 24 h earlier, as validated by nurses before starting the infusions. Thirteen (81.3%) of the 16 infusions (given to the 7 patients) were successful (no immediate or delayed HSR symptoms), but only four patients were retreated with oxaliplatin. No anaphylaxis or oxaliplatin-related death occurred during desensitization. Four patients were subsequently retreated with oxaliplatin-based regimens with 6-h infusion times after at least two successful desensitization protocols. Among the retreated patients, one patient had received the infusion over 2 h rather than 6 and had recurrent HSR. Among the other three patients transitioned from the desensitization procedure to a 6-h infusion, two had progressive disease and one neurosensitivity, which led to oxaliplatin discontinuation and treatment changes (Table 2). These outcomes suggest the importance of slowly infusing oxaliplatin over 6 h.

To our knowledge, this report is the first to highlight the safety and feasibility of oxaliplatin-desensitization protocols in a French outpatient cancer unit. The desensitization-procedure success rate was consistent with the literature [5, 6]. While there is no standard approach for oxaliplatin-desensitization regimens, some available parameters could help select patients. Among them, skin tests might be the most useful in stratifying patients mounting IgE-mediated HSRs to oxaliplatin-based regimens. In a prospective study, oxaliplatin-specific immunoglobulin-E was found to be a novel diagnostic tool for stratifying HSRs (100% specificity) [8]. The results of a recent retrospective study [9] suggested desensitization-procedure safety, regardless of oxaliplatin-infusion route, with high efficacy (76%) especially after severe grade 3/4 (79%) HSRs. One limitation of our study is the small number of patients included whose characteristics were examined retrospectively.

In conclusion, an oxaliplatin-desensitization procedure was feasible and safe in an outpatient cancer unit and could improve patients' quality of life and lower treatment-related costs. The success rate of these procedures could be further enhanced by refining patient-selection criteria for desensitization (according to initial HSR grade or diagnosis). Multicenter studies are warranted to confirm these results and standardize oxaliplatin-desensitization procedures as a routine outpatient practice in France.

Table 1 Oxaliplatin-desensitization protocol with progressive increase of the infusion rate

Time (h)	Infusion rate (mL/h)	Duration (min)	Total dose (%)
T 0	1	30	0.09
T 0.5	3	30	0.28
T 1	8	30	0.74
T 1.5	20	30	1.85
T 2	50	30	4.62
T 2.5	100	30	9.24
T 3	150max*	180	83.18
Total			100.00

*The infusion rate during the three last hours must be adapted according to the initial bag volume in order to respect a total infusion time of 6 h but must not exceed 150 mL/h

Table 2 Patients' characteristics

Characteristic	Patient						
	1	2	3	4	5	6	7
Age, years	72	62	62	83	33	72	48
Sex	Male	Female	Female	Male	Female	Male	Male
Known allergy	No	Yes (nickel)	No	No	No	No	No
Tumor location	Esophagus,	Esophagus	Esophagus	Esophagus	Colon	Colon	Stomach
Stage	Locally advanced	Locally advanced	Metastatic	Locally advanced	Metastatic	Metastatic	Metastatic
Chemotherapy regimen	5FU + oxaliplatin	5FU + oxaliplatin	5FU + oxaliplatin	5FU + oxaliplatin	5FU + oxaliplatin + panitumumab	5FU + oxaliplatin + bevacizumab	5FU + oxaliplatin + trastuzumab
Oxaliplatin infusions before HSR, *n*	2	2	7	4	7	6	5
Initial HSR grade	3	2	2	2	1	2	2
HSR clinical manifestations	Hypotension, urticaria, dyspnea	Rash	Rash, pruritus	Rash, pruritus, dyspnea	Pruritus	Rash, urticaria	Dyspnea
Skin test							
Yes/no	Yes	Yes	Yes	Yes	No	Yes	Yes
Positive/negative	Positive	Positive	Positive	Negative		Negative	Negative
Desensitization protocol, *n*	1	5	2	2	2	2	2
Premedication taken, Yes/no	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Recurrent HSR							
Yes/no	Yes	Yes	No	Yes	No	No	No
Grade	2	3		1			
Oxaliplatin retreatment* infusions, *n*	0	0	1	0	6	6	2
Outcome	Change treatment	Change treatment	Too short infusion (2 h) led to treatment change	Change treatment	Successful retreatment but progressive disease	Successful retreatment but progressive disease	Successful retreatment but neurotoxicity

5FU, 5-fluorouracil; HSR, hypersensitivity reaction

*The retreatment procedure consisted of a 6-h infusion of oxaliplatin with a constant flow rate

Acknowledgments We acknowledge Janet Jacobson, an English-speaking American scientist, for her review of our clinical report.

Data Availability The datasets used and/or analyzed during the current study are available from the corresponding author on reasonable request.

Compliance with ethical standards

Research involving human participants and/or animals For this type of study format consent is not required.

Informed consent For this type of study format consent is not required.

Conflict of interest Damien Botsen reports personal fees from Pierre Fabre and non-financial support from GlaxoSmithKline, Novartis, Chugai, and Amgen outside the submitted work.

Camille Mazza reports personal fees from Pierre Fabre outside the submitted work.

Mathilde Brasseur reports personal fees from Bayer and non-financial support from Pierre Fabre, Novartis, Amgen, Roche, and AbbVie outside the submitted work.

Olivier Bouche reports grants from Roche, personal fees from Roche, grants from Pierre Fabre, personal fees from Pierre Fabre, personal fees from Amgen, personal fees from Bayer, personal fees from Lilly, personal fees from Merck, personal fees from Novartis, outside the submitted work.

Elise Lepoix, Florian Slimano, and Anne Grange: none.

References

1. André T, Boni C, Mounedji-Boudiaf L, Navarro M, Tabernero J, Hickish T, Topham C, Zaninelli M, Clingan P, Bridgewater J, Tabah-Fisch I, de Gramont A (2004) Oxaliplatin, fluorouracil, and leucovorin as adjuvant treatment for colon cancer. N Engl J Med 350(23):2343–2351
2. Syrigou EI, Karapanagiotou EM, Alamara CV, Boura PG, Saif MW, Syrigos KN (2009) Hypersensitivity reactions to oxaliplatin: a retrospective study and the development of a desensitization protocol. Clin Colorectal Cancer 8(2):106–109
3. Brandi G, Pantaleo MA, Galli C, Falcone A, Antonuzzo A, Mordenti P, Di Marco MC, Biasco G (2003) Hypersensitivity reactions related to oxaliplatin (OHP). Br J Cancer 89(3):477–481
4. Hong DI, Dioun AF (2014) Indications, protocols, and outcomes of drug desensitizations for chemotherapy and monoclonal antibodies in adults and children. J Allergy Clin Immunol Pract 2(1):13–19 quiz 20
5. Castells MC, Tennant NM, Sloane DE, Hsu FI, Barrett NA, Hong DI, Laidlaw TM, Legere HJ, Nallamshetty SN, Palis RI, Rao JJ, Berlin ST, Campos SM, Matulonis UA (2008) Hypersensitivity reactions to chemotherapy: outcomes and safety of rapid desensitization in 413 cases. J Allergy Clin Immunol 122(3):574–580
6. Wong JT, Ling M, Patil S, Banerji A, Long A (2014) Oxaliplatin hypersensitivity: evaluation, implications of skin testing, and desensitization. J Allergy Clin Immunol Pract 2(1):40–45
7. National Cancer Institute Common Terminology Criteria for Adverse Events (CTCAE) Protocol Development (2010) | CTEP
8. Madrigal-Burgaleta R, Berges-Gimeno MP, Angel-Pereira D, Ferreiro-Monteagudo R, Guillen-Ponce C, Pueyo C, Gomez de Salazar E, Alvarez-Cuesta E (2013) Hypersensitivity and desensitization to antineoplastic agents: outcomes of 189 procedures with a new short protocol and novel diagnostic tools assessment. Allergy 68(7):853–861
9. Le Roy F, Rigault E, Regnault D, Hubert N, Burtin P, Hollebecque A, Malka D, Boige V, Ducreux M (2018) Oxaliplatin desensitization after hypersensitivity reaction: a single-center experience on more than 300 procedures. J Clin Oncol 36(4_suppl):610–610