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# **Allergy evaluation of hypersensitivity to platinum salts and taxanes: a six-year experience.**

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1 ABSTRACT

2 **BACKGROUND:**

3 Hypersensitivity reactions (HSRs) to platinum salts (PS) and taxanes (TX) are a challenge to  
4 cancer management. Allergy evaluation based on skin tests (ST) and graded challenges can  
5 provide a diagnosis of an allergy to a suspected drug and indicate possible treatment with  
6 alternative same-class drugs.

7 **OBJECTIVE:**

8 This study aimed to estimate the negative predictive value of ST in the diagnosis of HSRs to  
9 TX and PS.

10 **METHODS:**

11 This multicenter study prospectively enrolled patients with a suspected HSRs to PS and TX.  
12 ST were performed for chemotherapy, drugs of the same pharmacological class and other  
13 agents (latex or co-treatments). For patients with negative ST, a graded challenge was  
14 performed by the cancer teams trained in allergy management.

15 **RESULTS:**

16 A total of 119 consecutive patients were included during a six-year period. ST results were  
17 positive for 58% of the cohort: for TX in 7 patients and for PS in 62 patients. Other agents  
18 were responsible for 4.2% of cases. Skin cross-reactivity were 50% for TX and 30% for PS. A  
19 graded challenge was performed in 14 patients for TX and in 50 patients for PS. Negative  
20 predictive values (NPV) for ST were 100% for TX and 92% for PS, with NPVs for  
21 individuals PS of 100% for cisplatin, 89% for oxaliplatin and 87% for carboplatin.

22 **CONCLUSIONS:**

23 ST to PS or TX offered a high NPV, making allergy evaluation a key element in the  
24 management of cancer patients. Graded challenges can be safely performed by oncology  
25 teams trained in anaphylaxis management.

26

27 **HIGHLIGHTS BOX**

28

29 **What we already know about this topic?**

30 Allergy to PS and TX is among the most frequent side-effect of chemotherapy. Allergy  
31 evaluation is an essential element in the management of cancer patients

32 **What does this article add to our knowledge?**

33 A standardized allergy workup for PS and TX identified 63% of patients with HSR to PS,  
34 33% to TX and 4.2% to concomitant drugs. The NPV of ST was excellent reaching 92% for  
35 PS and 100% for TX.

36 **How does this study impact current management guidelines?**

37 Allergy evaluation for PS and TX hypersensitivity should be reliably integrated into the  
38 therapeutic management of patients. Graded challenges can be delegated to cancer teams,  
39 provided they are experienced in managing anaphylactic reactions.

40

41 **KEY WORDS:** Chemotherapy; Drug allergy; Graded challenge; Skin tests; Taxanes;

42 Platinum salts

43

44

45 **ABBREVIATIONS USED:**

46 CAR: carboplatin

47 CIS: cisplatin

48 DOCE: docetaxel

49 GC: graded challenge

50 GCP: graded challenge performed

51 GCT: graded challenge tolerated

52 ID: intra-dermal reaction test

53 NPV: negative predictive value

54 OXA: oxaliplatin

55 PACLI: paclitaxel

56 PS: platinum salts

57 SPT: skin prick test

58 ST: skin test

59 TX: taxanes

## 60 INTRODUCTION

61 Improved diagnosis and care of patients with cancer has resulted in better patient survival and  
62 longer treatment. Patients are thus exposed more frequently and for longer periods of time to  
63 chemotherapy. This situation increases the risk of hypersensitivity reactions (HSRs) to  
64 chemotherapy and constitutes a challenge to cancer treatment (1,2).

65 Although allergies to platinum salt (PS) are most often IgE-mediated, mixed reactions  
66 associating symptoms suggestive of both IgE and non-IgE-mediated reactions have been  
67 reported (3). Anaphylatoxins such as C3a and C5a, generated by immune complexes, can  
68 induce mast cell degranulation, a mechanism that has already been described for vancomycin,  
69 iodinated contrast agents and formulation vehicles (such as Cremophor EL, polysorbate 80  
70 and polyethylene glycol), which can be found in TX and other drugs (4).

71 PS-related HSRs have an incidence of 12 to 17 %, with carboplatin being the most frequent (9  
72 – 27 %), followed by cisplatin (5 – 20 %) and oxaliplatin (10 – 19 %) (3,5). Symptoms often  
73 start between the 4<sup>th</sup> and the 10<sup>th</sup> dose, and risk factors such as female gender, a platinum-free  
74 interval of more than 1 year, and the presence of *BRCA1/2* mutations in carboplatin  
75 hypersensitivity have been reported (6). The incidence of TX-induced HSRs varies from 10 to  
76 70 % (7,8). Non-allergic HSRs are more common, which explains why symptoms often start  
77 after the first or second exposure (4).

78 With limited anti-neoplastic therapeutic options, being able to accurately identify  
79 hypersensitivity is crucial to decrease unnecessary desensitizations. There is a need for tests  
80 with high negative (NPV) and positive predictive values (PPV) (9). According to EAACI  
81 guidelines, skin tests (ST) are useful for PS-related HSRs (10). Their sensitivity is 66 % for  
82 cisplatin and 100 % for carboplatin and oxaliplatin, with a NPV of 94 % (11). Prior studies  
83 suggested that ST for PS can be useful to stratify the risk after HSRs identifying patients who  
84 require desensitization from those who can be safely re-challenged (12,13). For others, neither



85 clinical characteristics nor ST results predicted outcomes, thus desensitizations are used in all  
86 patients with immediate HSR history (14).

87 The value of ST in TX-related HSR is less well documented and authors suggested that a  
88 clinical approach could be sufficient for risk stratification (15).

89 In this study, we report our comprehensive experience of allergy evaluation of patients with  
90 suspicion of PS or TX hypersensitivity. The study was conducted for 6 years at the University  
91 Hospital Center of Nice.

## 92 **METHODS**

### 93 **STUDY DESIGN AND OBJECTIVES**

94 We conducted a multicentric observational cohort study including adult patients who  
95 presented with suspicion of PS or TX hypersensitivity, from July 2012 to July 2018. ST and  
96 desensitization were conducted in the Allergy Department at the Nice University Hospital.  
97 Graded challenges (GC) were performed in two separate oncology centers in Nice (the  
98 Antoine Lacassagne anti-cancer center and the Oncology unit at the Nice University Hospital  
99 Center). All the patients who received an allergy evaluation gave their informed consent for  
100 clinical data collection and GC.

101 The main objective of this study was to evaluate the NPV of ST for the diagnosis of  
102 hypersensitivity to PS or TX. Secondary objectives were to assess the feasibility of delegating  
103 GC to two different oncology teams, to analyze the characteristics of hypersensitivities to PS  
104 or TX and to identify patient phenotypes.

105

### 106 **MATERIALS AND ALLERGY EVALUATION**

107 All adult patients referred for assessment of hypersensitivity to TX and/or PS were included.  
108 Immediate reactions were defined by the occurrence of allergic clinical features at infusion

109 and up to one hour later. The severity of immediate reactions was defined according to the  
110 Ring and Messmer's classification (16). We distinguished mild allergic reactions (grade I)  
111 from anaphylaxis (grades II-IV).

112 All patients with an immediate reaction underwent both skin prick tests (SPT) and intra-  
113 dermal tests (ID) for co-treatments, latex, and PS or TX as applicable, according to the  
114 European Network for Drug Allergy/European Academy of Allergy and Clinical Immunology  
115 (ENDA/EAACI) recommendations (10).

116 The SPT concentrations for carboplatin, cisplatin, oxaliplatin, docetaxel and paclitaxel were  
117 10, 1, 5, 10 and 6 mg/ml respectively. IDs started at 1/1000<sup>th</sup> up to a maximum of PT  
118 solutions. Whatever the SPT result, ID were performed to validate the SPT reaction, and to  
119 define the cutoff values for ID reactivity. A weal of 3 mm or more in diameter for SPTs or an  
120 increase in diameter of the initial ID of 3 mm or more were defined as a positive test,  
121 provided that the two conditions, (i) a negative response to control solution (0.9% saline) and  
122 (ii) a positive response to histamine (SPT: 10 mg/mL) were satisfied.

123 Depending on the results of ST, three proposals were made:

- 124 1. Negative ST to the suspected drug: a GC was performed as described below.
- 125 2. Positive ST to the suspected drug and negative ST to an alternative same-class  
126 chemotherapy agent: the alternative drug was suggested to clinicians using the GC  
127 described below.
- 128 3. Positive ST to the suspected drug in the absence of possible alternatives: a 7-step rapid  
129 desensitization protocol of 330 minutes duration using incremental doses, adapted  
130 from 12-step protocol described by Castells *et al.* (5), was implemented in our allergy  
131 unit.

132 All GCs were done in one of two distinct oncology departments, where the staff were trained  
133 to rapidly identify and treat anaphylaxis. To further standardize reintroduction, four parenteral

134 preparations with progressive concentrations (1/1000, 1/100, 1/10, recommended  
135 concentration) were prepared and dispensed by the hospital's central pharmacy. The lower-  
136 concentration infusion bags were infused over 15-minute and the parenteral preparation at the  
137 recommended concentration was administered according to the manufacturer's instructions.  
138 The monitoring was extended by 2 hours. If patients had no reaction during GC, they were re-  
139 introduced as standard regimens.

140 For patients with late reactions, late ID and patch tests were performed with the suspected  
141 chemotherapy and co-treatments. Readings were then performed at 15-20 minutes (immediate  
142 reading of ID), and 48-72 hours later (Patch tests and ID). The dilutions for delayed reading  
143 ID were similar to immediate ID. Patch and delayed reading of ID were scored as  
144 recommended by Johansen *and al.* (17). Reintroduction was proposed for causative  
145 chemotherapy or an alternative depending on the negative ST results and only for mild late  
146 clinical reactions.

147

148

149 **STATISTICAL ANALYSES:**

150 Data are presented as n (%) for categorical variables and as mean  $\pm$  SD for continuous  
151 variables. The NPV of immediate reading of ST for PS or TX was defined as the proportion  
152 of non-allergic patients (i.e. patients tolerating chemotherapy drug reintroduction), among the  
153 patients with negative immediate reading ST. The NPV was calculated for each chemotherapy  
154 drug and each chemotherapeutic drug class. Comparisons were made for categorical  
155 variables by using nonparametric tests. A P value of less than .05 was considered significant.

156 All analyses were performed using the Statistical Package for the Social Sciences (SPSS®)  
157 statistical software (IBM Corp. Released 2017. IBM SPSS Statistics for Windows, Version  
158 25.0. Armonk, NY).

## 159 RESULTS

160 A total of 119 consecutive patients were admitted for an allergy evaluation (98 for PS only,  
161 20 for TX only, and one for both) over six years. Fifty-two percent of the patients underwent  
162 an allergy workup within the last two years of this study. Forty-three percent of the  
163 malignancies were gynecological (35 ovarian, 5 uterine, 11 breast cancers), 43 % digestive  
164 (28 colorectal, 11 pancreatic, 5 stomach, 4 biliary duct cancers, 3 esophageal) and 14 %  
165 cancers of the airways (ENT and lung).

166 One hundred and ten patients (92%) experienced immediate hypersensitivity, with various  
167 grades of severity (distribution shown in figure 1). More than 50% of these patients had  
168 anaphylaxis. Immediate HSR of ten patients (9%) consisted of fever and/or chills. The sex  
169 ratio was 3.4 (92 women; 27 men), due to the frequent use of PS and TX in gynecological  
170 malignancies, especially since relapse is also treated using the same chemotherapeutic drug  
171 classes. The number of cycles before the development of HSR, as well as the interval between  
172 the previous dose and the agent responsible of the HSR are reported in table I.

173 The allergy evaluation for immediate HSR is presented as flow diagrams for PS (figures 2)  
174 and TX (figure 3). ST were positive in 69 patients (58%) of the total cohort: TX for 7/21  
175 patients (docetaxel [n=2], paclitaxel [n=5]) and PS for 62/99 patients (oxaliplatin [n=34],  
176 carboplatin [n=24], cisplatin [n=4]). Other agents (latex, co-treatments) were responsible for  
177 an additional 4.2% of cases. For immediate HSRs (110 patients), 61% had positive ST for the  
178 suspected chemotherapy drug and 3.6% for co-treatments. Most immediate chemotherapy  
179 drug allergies were identified by means of ID (17 SPT and 67 ID). For PS, the results of SPT  
180 and ID were in agreement (i.e. positive SPT and ID) but SPT had a lower sensitivity than ID,  
181 as expected. We noted that SPT were always negative for TX.

182

183 **Patients with a suspected allergy to platinum salts.**

184 Among the patients with a PS-related HSR, 92/99 (92.9%) had immediate reactions of which  
185 61/92 (66.3%) had a positive ST for the suspected chemotherapeutic drug, with 4 reactions to  
186 cisplatin (0 SPT, 4 ID), 23 to carboplatin (5 SPT, 23 ID) and 34 to oxaliplatin (12 SPT, 34  
187 ID). An interval of  $35 \pm 25$  days between the suspected anaphylaxis and the ST was noted for  
188 these 92 patients. Due to the urgency of therapeutic treatment, 5/92 (5.4%) of these patients  
189 had an allergy evaluation done less than 10 days after the suspected anaphylaxis. These 5  
190 patients showed an initial negative ST, with a recurrent reaction when the suspected  
191 chemotherapy was reintroduced. The deferred tests later confirmed hypersensitivity. All other  
192 patients waited at least 14 days between the suspected anaphylaxis and ST.

193 In 18/61 (30%) patients with a positive ST to the suspected PS, a positive ST to another PS  
194 was identified. Cross-reactions were not observed when the suspected drug was cisplatin.  
195 When the suspected drug was oxaliplatin, there was no cross-reactivity with cisplatin but 18%  
196 for carboplatin. For carboplatin, cross-reactivity with cisplatin was observed in 4% and with  
197 oxaliplatin in 48% of ST.

198 As shown in table 1, patients with a positive ST had more severe immediate reactions to PS  
199 compared to patients with a negative ST (74% vs 29% anaphylaxis of grade II or higher  
200 ( $p=0.0003$ )). Nonetheless, 44% of grade 1 reactions had a positive ST. Fifty patients with a  
201 negative ST had PS reintroduced (25 with the same PS and 25 with an alternative PS). Graded  
202 challenge with PS induced no reaction for cisplatin in 17 patients, 2 reactions for carboplatin  
203 in 15 patients and 2 reactions for oxaliplatin in 18 patients. Reactions observed during  
204 reintroduction were grade 1 in 3 patients and grade 2 in 1 patient. Patients who tolerated GC  
205 were all subsequently reintroduced without reaction. Thus, the NPV of ST for PS was 92%.  
206 For each PS, NPVs were as follows: 100% for cisplatin, 89% for oxaliplatin and 87% for  
207 carboplatin.

208 In 16 patients with a confirmed allergy to PS, a desensitization schedule was proposed. The

209 full dose could be administered in 87% of patients; 3 mild reactions were treated with a  
210 slower infusion rate and 1 moderate reaction required a one-hour break from infusion,  
211 additional medication and a significantly slower infusion rate. For the remaining 2 patients  
212 (13%), the procedure was definitively stopped due to a severe reaction despite premedication  
213 and slower infusion rates.

214

#### 215 **Patients with a suspected allergy to taxanes.**

216 Among the 21 patients with suspected reactions to TX, 18 (85.7%) had an immediate and 3  
217 (14.3%) had a delayed reaction. The interval between HSR and ST was  $41 \pm 19$  days. Six  
218 patients (33.3%), had positive immediate ID readings: 5 for paclitaxel and 1 for docetaxel  
219 with a cross-reactivity of 50% for paclitaxel with docetaxel. One patient had an immediate  
220 allergic reaction to ranitidine (co-treatment). All patients with a ST positive for TX  
221 experienced at least grade II anaphylaxis versus 40% of ST-negative patients ( $p=0.03$ ).  
222 Fourteen patients with a negative ST had TX reintroduced (12 with the same TX and 2 with  
223 an alternative TX). Graded challenge with TX did not induce a reaction to paclitaxel in 12  
224 patients and docetaxel in 2 patients. All patients except one (died) who tolerated GC were all  
225 subsequently reintroduced without reaction. Thus, the NPV of ST for TX was 100% in our  
226 cohort. For TX-related HSRs, only one patient underwent desensitization to paclitaxel,  
227 without a subsequent reaction.

228

#### 229 **Patients with a suspected allergy to concomitant agents.**

230 Five patients of the cohort (4.2%) had a positive ST for concomitant agents. Four of them had  
231 immediate reactions and a positive ST to methylprednisolone, clindamycin, ranitidine, and  
232 latex. The latter two were also found to have a positive ST for PS. The fifth patient had a late  
233 positive ST for clindamycin.

234

**235 Patients with delayed hypersensitivity reactions.**

236 Ten patients of the cohort (8.4%) had a delayed hypersensitivity reaction. Seven cases (70%)  
237 were PS-related: one patient with Drug Rash with Eosinophilia and Systemic Symptoms  
238 (DRESS), five patients with a maculopapular rash, and 1 patient with delayed urticaria (48  
239 hours). Three cases (30%) were TX-related (delayed urticaria [24 hours]).

240 For PS-delayed HSRs, one out of the five patients with a maculopapular rash had positive  
241 delayed-reading ID for carboplatin with cross-reactivity with oxaliplatin, and another patient  
242 had a positive patch test for clindamycin. The chemotherapy drug was therefore reintroduced  
243 according to a GC in all 4 patients with a negative delayed-reading ID, without subsequent  
244 symptoms. In the patient presenting with a DRESS syndrome, although ST were negative, the  
245 suspected drug was not reintroduced.

246 For TX-delayed HSRs, one of the three patients had a positive delayed-reading ID for  
247 docetaxel without cross-reactions to paclitaxel, which was reintroduced without complication.  
248 Paclitaxel was reintroduced to the second patient with negative ST without complications.  
249 The third patient benefited from a change in chemotherapy.

250



## 251 **DISCUSSION**

252 Hypersensitivity to PS and TX is well recognized. This comprehensive study conducted over  
253 6 years confirmed the increase in referrals for a chemotherapy drug allergy evaluation in our  
254 institution. This highlights the need for a feasible and standardized workup that can be  
255 integrated into the patient's oncological care protocol. Many patients had positive ST to the  
256 implicated chemotherapeutic agent (33% for TX ; 63% for PS) or other agents (4.2%),  
257 confirming the relevance of patients selection referred for an allergy evaluation. To put this  
258 into perspective, the rate of positive ST to  $\beta$ -lactam antibiotics in patients referred for a  $\beta$ -  
259 lactam allergy workup, in our experience and that of others, is as low as 20 % (data not  
260 shown) (18,19).

261 The requests for an allergy evaluation were dominated by immediate reactions (92% of  
262 cases). We chose Ring and Messmer's classification to differentiate true anaphylaxis (grades  
263 II-IV) from mild reactions (grade I), which are not identified in Sampson's grading of  
264 anaphylaxis (20). Most of the documented allergic reactions to PS and TX were immediate  
265 HSR, most of which were severe (55% for PS and 50% for TX). Grade III and IV were the  
266 most frequent (57%), with two patients suffering from successfully-resuscitated  
267 cardiorespiratory arrest. These data are in agreement with the literature, which report that  
268 most of the PS- and TX-related HSR are severe and require diagnostic confirmation.  
269 Therefore, it is crucial to detect, as early as possible, clinical manifestations suggestive of an  
270 allergy, especially since some symptoms such as fevers or chills (9 % of patients with PS-  
271 related HSR) may be mistakenly diagnosed as due to infection (11,21). As in similar studies,  
272 HSR often occurred around the 8<sup>th</sup> infusion of the chemotherapy drug (3,5,21,22). In  
273 combination treatments containing PS, after a treatment pause (chemotherapy-free interval) of  
274 2 years and longer, the rate of HSR increased (3,5,11). Currently, routine screening ST are not  
275 done in patients requiring resumption of treatment with a PS. A more thorough analysis of the

276 characteristics of patients with and without HSR during renewed treatment may help identify  
277 the predisposing factors (6,23).

278 The validity of ST varies according to the published data. The primary outcome of our study  
279 was to measure the NPV of ST on immediate reading, which was excellent, reaching as high  
280 as 92% for PS and 100% for TX for our selected cohort. This high NPV for PS ST should  
281 only be expected when a minimum interval of 2 weeks has been observed between the HSR  
282 and the allergy evaluation. This work also demonstrated the reliability of the decision-making  
283 algorithm, which showed that GC based on the results of ST was applicable even to severe  
284 grade III and IV anaphylaxis reactions. This was not the case for all the studies on this subject  
285 where chemotherapy was not reintroduced if the grade of the anaphylactic reaction was III or  
286 higher (24,25). The choice of our 4 step-GC can also be debated for PS and TX. Indeed,  
287 similar protocols are proposed as desensitization processes for cases of mild HSR to PS (26).  
288 First, our dilutions are about different from those previously published with higher steps  
289 and/or a shorter infusion time. Second, these studies excluded ST, suggesting that a number of  
290 patients were not allergic. In addition, our patients with GCT subsequently tolerated their  
291 usual infusion, confirming that our 4-step-GC was not a test that mimicked the desensitization  
292 process but an effective and safer re-challenge test (27).

293 Based on clinical symptoms and initial HSR, authors suggested that a re-challenge can be  
294 safely proposed for TX without any ST (28). This strategy would have potentially exposed  
295 33% of our TX cohort to the same or even more severe HSR. Others proposed a re-challenge  
296 test for TX or PS with an infusion rate similar to standard regimen (12). Even, if only mild  
297 reactions were found in 49% of re-challenges, up to 11% experienced a severe reaction. This  
298 approach cannot be safely proposed outside expert centers (12).

299

300 Regarding cross-reactions between PS, our ST also showed an excellent NPV allowing for

301 safe reintroduction of the alternative drug (29). We confirmed, as previously observed, no  
302 cross reactivity between cisplatin and oxaliplatin (30,31). However, oncological teams  
303 sometimes considered that cisplatin is a reasonable approach for continuing platinum-based  
304 chemotherapy in patients with a significant carboplatin or oxaliplatin HSRs provided it has  
305 never been used before (31,32). The relevance and reliability of ST must therefore be  
306 reiterated to convince cancer teams to include this approach into patient care and to perform  
307 additional studies to address these questions. In the case of delayed reactions, the limited  
308 number of cases precluded validation of this approach but it seems necessary to extend the  
309 experiment along this line.

310

311 A secondary objective of our study was to analyze the relevance of the stepwise approach for  
312 ST (SPT and ID for all drugs of the same pharmacological class). As reported by other  
313 authors, SPT for TX did not provide any added value to ID alone given that all of them were  
314 negative (24,25). The severity of the initial HSR seems to be associated with a higher rate of  
315 positive ST for both PS and TX. However, a PS-related allergy has been demonstrated in 44  
316 % of patients with a mild clinical reaction (Grade I). This stage of reaction is often  
317 underestimated and treated symptomatically, exposing the patient to the risk of a more severe  
318 subsequent reaction. Our data confirmed that the cross-reaction rate of same-class drug  
319 allergies is around 30 % for PS (mostly between carboplatin and oxaliplatin), and 50 % for  
320 TX (3,8,33). Although allergies to co-treatments or latex were rare (4.2 % of patients), they  
321 should still be necessarily investigated.

322 The present study also demonstrated the feasibility of delegating drug GC reintroduction to  
323 cancer teams after a negative allergy evaluation. Among 64 patients, only 4 (6.3%) had  
324 relapsing HSR. All reactions were grade II or less. This strategy appears to be safe and  
325 effective provided: 1) medical and paramedical cancer teams were trained to recognize and

326 treat anaphylaxis, 2) a secure procedure for drug dispensation at the desired dilutions exists in  
327 the hospital's central pharmacy, 3) written information concerning the allergy evaluation was  
328 given, and 4) informed consent was obtained from the patient.

329 Our department evaluated the risk and burden of desensitization protocols for first  
330 administration to patients, rather than assigning this step to the cancer teams. This may be  
331 approached differently by other teams, depending on the strategy and the protocols of each  
332 center, and the availability and the knowledge of the teams. The success rate and the safety of  
333 our protocols, especially for PS, was high. This is in agreement with the current literature  
334 (5,34–37). We used a 7-step rapid desensitization protocol, although most authors use the 12-  
335 step protocol initially used by Castell *et al.* (38). Our protocol used the same total duration of  
336 administration (330 minutes) but with fewer dilutions.

337

338

339 **CONCLUSIONS**

340 Allergy evaluation for PS and TX hypersensitivity can be reliably integrated into the  
341 therapeutic strategies of patients. The NPV was excellent for TX and PS if a minimum of a  
342 14-day period was observed between the reaction and ST. Graded challenges can be safely  
343 performed by oncology teams provided they are trained to recognize and manage anaphylactic  
344 reactions.

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## TABLE AND FIGURE LEGENDS

### **Table I: Patient characteristics and results of skin tests**

Characteristics of patients, clinical reactions and chemotherapy involved in hypersensitivity reactions according to the result of skin tests. Severity grades follow the Ring and Messmer's classification for immediate hypersensitivity reactions.

### **Figure 1: Hypersensitivity reactions to platinum salts and taxanes**

Percentage of patients examined for a platinum salt and taxane allergy according to the type of clinical reaction. Immediate reactions are classified according to the Ring and Messmer's classification. Other reactions were delayed or unclassifiable.

### **Figure 2: Flow diagram for immediate hypersensitivity to platinum salts**

Flow diagram showing step by step management of suspected immediate hypersensitivity to platinum salt after reading the results of skin tests to PS. If a PS graded challenge was performed (GCP), we recorded those who tolerated the full dose of treatment (GCT).

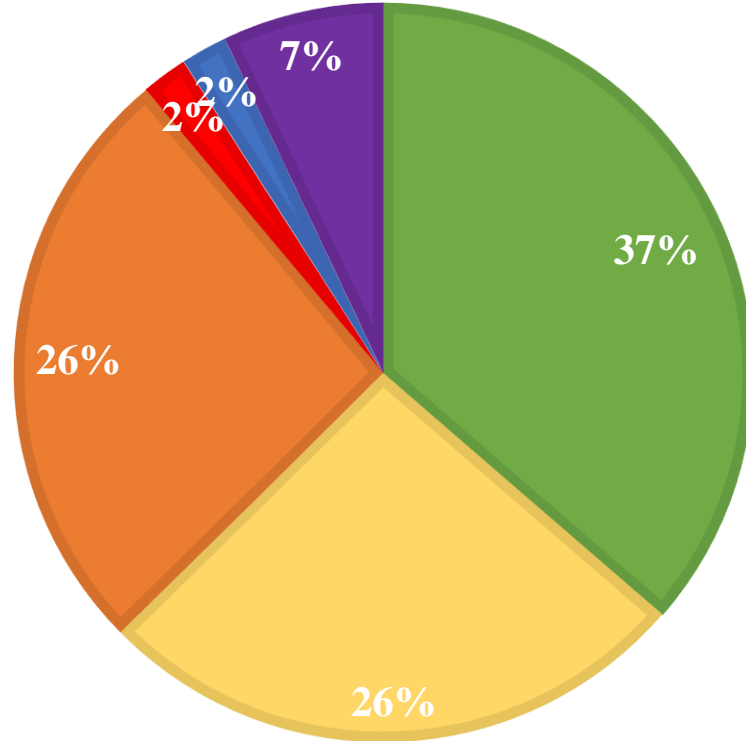
### **Figure 3: Flow diagram for immediate hypersensitivity to taxanes**

Flow diagram showing step by step management of suspected immediate hypersensitivity to taxanes after reading the skin test results for TX. If a TX graded challenge was performed (GCP), we recorded those who tolerated the full dose treatment (GCT).

# **Figure 1: Hypersensitivity reactions to platinum salts and taxanes**

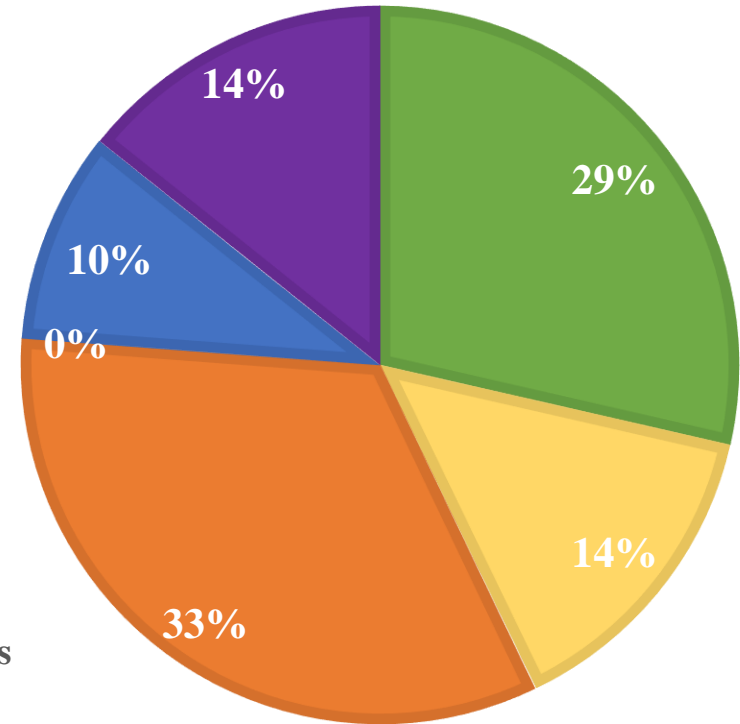
## Platinum Salts

(n=99)



## Taxanes

(n=21)



- Grade I
- Grade II
- Grade III
- Grade IV
- Unclassifiable
- Delayed reactions

## **Figure 2 : Flow diagram for immediate hypersensitivity to platinum salts**

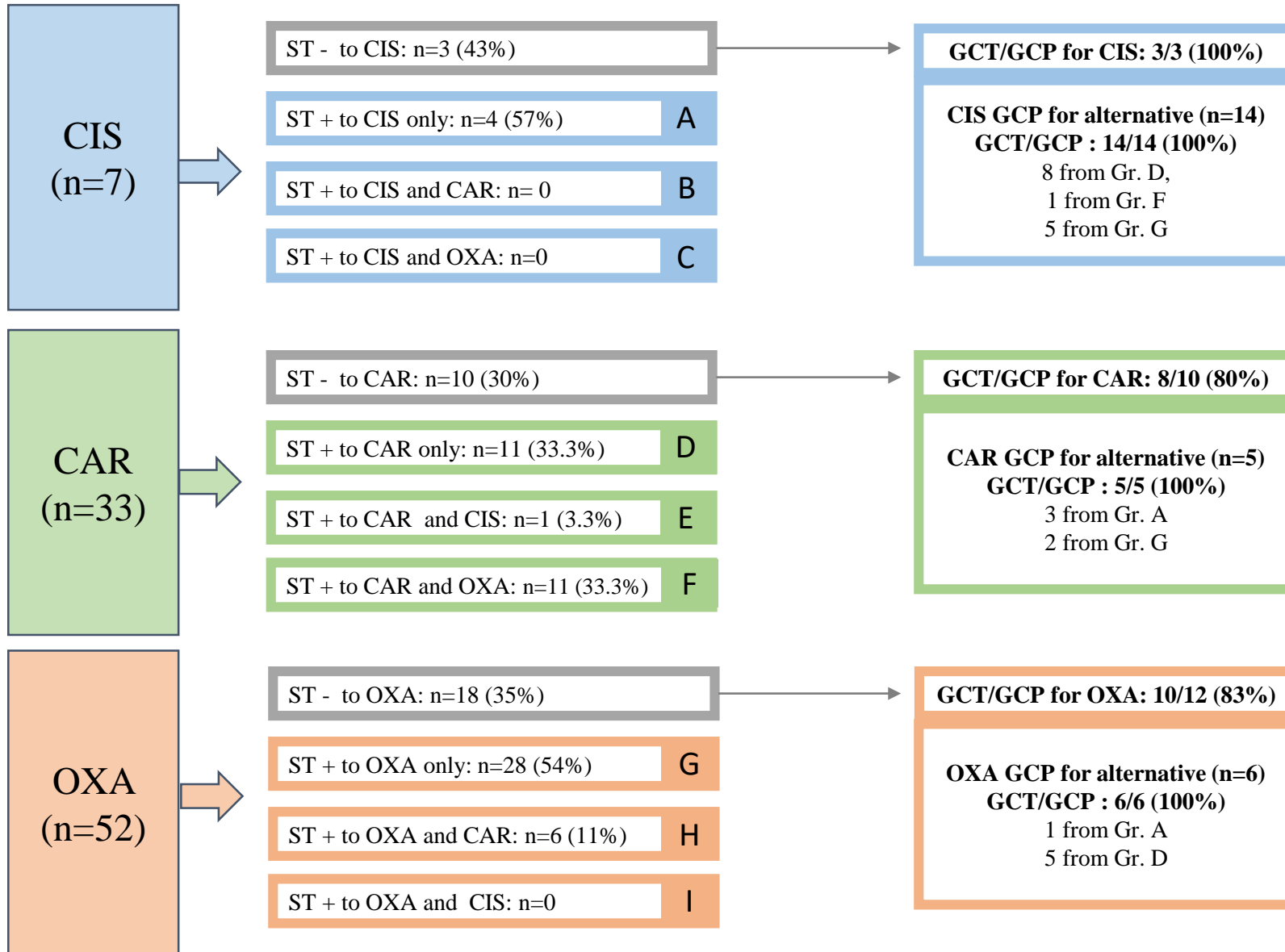
*CAR : carboplatin ; CIS: cisplatin ; GCP : graded challenge performed ; GCT : graded challenge tolerated;*

*OXA: oxaliplatin ; ST: skin tests*

Immediate HSR to Platinum Salts

Step 1 : Skin tests and groups

Step 2 : Graded challenges





# Figure 3 : Flow diagram for immediate hypersensitivity to taxanes

*DOCE: docetaxel ; GCP : graded challenge performed ; GCT : graded challenge*

*tolerated; PACLI: paclitaxel ; ST: skin tests*

Immediate HSR to Taxanes

