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Eligibility criteria to cisplatin in head and neck squamous cell carcinoma: Egyptian expert opinion

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Abstract

Introduction: The use of cisplatin in clinical practice in the management of head and neck squamous cell carcinoma (HNSCC) is limited by its toxicity and acquired resistance, which makes the decision-making process of its prescription multifactorial.

Methods: An Egyptian expert panel (comprising nine Egyptian oncologists) meeting was held after a comprehensive literature review on the use of cisplatin in HNSCC. The panel aimed to develop a consensus on evidence-based recommendations for receiving cisplatin in the chemoradiotherapy management of HNSCC in Egyptian clinical practice.

Results: The panel indicated that an Eastern Cooperative Oncology Group Performance Status (ECOG PS) > 2, creatinine clearance (CCR) < 50 ml/min, neuropathy grade ≥ 2, pre-existing hearing loss or tinnitus ≥2, hematological problems (platelets < 100,000/mm^3, neutrophils < 1500/mm, and hemoglobin < 9 g/dl), and heart failure of New York Heart Association Classes III or IV (even if cardiovascular therapy is optimized); are all absolute contraindications to receiving cisplatin. On the other hand, relative contraindications to cisplatin according to the panel were an ECOG PS of 2, age more than 70 years, CCR between 50 and 60 ml/min, grade 1 neuropathy, grade 1 hearing loss, involuntary weight loss of ≥20% of body weight, Child–Pugh Scores B and C, previous induction chemotherapy, and heart failure of New York Heart Association Classes I or II with left ventricular ejection fraction ≤50%. The panel agreed that the socioeconomic status of patients should be considered when prescribing cisplatin to HNSCC patients.

Conclusion: Our discussion resulted in a set of evidence-based recommendations for cisplatin eligibility criteria in patients of HNSCC in Egypt.

KEYWORDS
cancer, cisplatin, Egypt, HNSCC

1 | INTRODUCTION

Head and neck cancers (HNCs) are considered the seventh most common type of cancer worldwide.[1] According to GLOBOCAN worldwide statistics, HNCs represented 8% of newly reported cancer cases and caused 10.2% of deaths among all cancer types in 2020.[2] Additionally, HNCs are predominant in developing countries as a result of several factors including poverty, illiteracy, and poor healthcare access; they also tend to present at advanced stages.[3]

Around 85% of HNCs are histologically squamous cell carcinoma.[4] Head and neck squamous cell carcinoma (HNSCC) arises from mucosal surfaces of the oral cavity. They can form in different locations including the lip, oral cavity, nasopharynx, oropharynx, hypopharynx, larynx, paranasal sinuses, and salivary glands.[5–9]

Known risk factors of HNSCC include smoking, alcohol consumption, Epstein–Barr virus, and human papillomavirus (HPV).[9] Bose et al.[5] threw light on the synergistic action of smoking together with alcohol consumption in inducing HNSCC, and such correlation led to significant public health implementations to diminish tobacco use. Consequently, a reduction in the incidence of HNSCCs was noted especially in developed countries.[5]

On the basis of reports of the World Health Organization (WHO), Guo et al.[6] estimated that 439,000 cancer cases of the mouth and the oropharynx will be reported by 2030. In 2016, Patterson et al. explicated the global burden of HNCs in terms of their economic burden along with mortality-to-incidence ratios. They found that the predictive value of HNC mortality in Egypt is expected to be 1916.16 cases by 2030, while the economic loss is predicted to be $2093.39 million from 2018 to 2030.[10] Additionally, the disease has debilitating effects on the quality of life (QoL); these include swallowing difficulties, nutritional problems, and visible disfigurement.[11] Given these predictions and disease impacts, attention to the appropriateness of treatment approaches is crucial.

The treatment of HNSCC is multimodal; it includes surgery, chemotherapy, and radiation. It aims at keeping both functionality and morphology of organs.[12] Platinum-based chemoradiotherapy (CRT) is the treatment of choice in locally advanced HNCs with a 5-year survival rate of 32% to 40%.[4] Also, the risk of death from HNCs is significantly reduced by 19% with CRT compared with radiation monotherapy (hazard ratio [HR] = 0.81, $p < 0.001$); however, CRT is associated with several acute and chronic toxicities.[13]

Cisplatin is the first-choice chemotherapeutic agent in the CRT management of HNSCC.[14] Cisplatin is immediately activated after entering cells where its hydrolyzation through exchanging chloride atoms with water molecules takes place. A such exchange makes cisplatin a very potent electrophile, that is, ready to attract nucleophiles. Subsequently, cisplatin binds purine residues' N7 reactive center causing DNA damage, division block, and cancer cell apoptosis.[15]

Nevertheless, the use of cisplatin is limited by its toxicity-induction capabilities and acquired resistance in clinical practice, which makes the decision-making process of prescribing cisplatin multifactorial. Hence, it is necessary that oncologists practice precision-based medicine and individualize cisplatin prescriptions according to the characteristics and goals of each patient.[12] Attempts have been taken to devise clear management approaches and possible alternatives; examples include the expert panel opinions conducted in Brazil and the Asia-pacific region.[16,17]

This Egyptian expert panel was conducted to devise evidence-based cisplatin eligibility criteria in the CRT management of HNSCC patients to come out with better treatment outcomes and minimal reductions in QoL. Factors such as age, comorbidities, organ dysfunctions, Eastern Cooperative Oncology Group Performance Status (ECOG PS) score, concomitant medications, and prior platinum-based chemotherapy are addressed and considered whenever cisplatin is employed in HNSCCs.[16,17] Accordingly, management of HNSCC with cisplatin is a challenging multifactorial process and should be individualized according to patients' conditions and treatment goals.[17,18]

2 | MATERIALS AND METHODS

Nine Egyptian oncologists were invited to this expert panel. All of them have been involved in the clinical management of HNSCC on a daily basis in Egypt. The discussion aimed at establishing evidence-based recommendations after reviewing the literature pertaining to cisplatin use in CRT management of HNSCC. Addressed points included cisplatin-induced toxicities, risk factors, doses, comorbidities, social and nutritional support, and alternative treatment options. The expert panel meeting was conducted in March 2021 and based on the experts' input and discussion, evidence-based recommendations were established.

3 | RESULTS AND DISCUSSION

According to the National Comprehensive Cancer Network (NCCN) guidelines of HNCs of 2021, high-dose cisplatin (100 mg/m^2 every 3 weeks) along with radiotherapy (RT) are the cornerstones in managing HNCs. However, such treatment modality is accompanied by acute and chronic toxicities; so, a low-dose once weekly cisplatin dose was suggested instead.[14] An Indian phase III randomized noninferiority trial compared the locoregional control (LRC) of two doses of cisplatin: the high dose (100 mg/m^2 once every 3 weeks) and the low dose (30 mg/m^2 once weekly). Results showed a significantly higher LRC rate in the high-dose setting than in the low-dose one (73.1% and 58.5%, respectively). However, the incidence of acute toxicities (Grade ≥ 3) was significantly more predominant in the high-dose arm than in the low-dose one (84.6% and 71.6%, respectively).[19]

Consequently, the decision-making process in patients with HNCs should be taken with caution, in terms of considering patients' characteristics and their treatment goals, susceptibility to acquiring toxicities of cisplatin, along with the most appropriate alternative treatment approaches.

The panel experts discussed the main points of consideration to determine the eligibility criteria for receiving cisplatin. These included ECOG PS, age, nephropathy, neuropathy, audiometry, previous treatment with platinum-based chemotherapy, involuntary weight

loss, hepatic impairment, hematologic toxicities, socioeconomic status, and congestive heart failure (CHF). A summary of the panel's recommendations is shown in Table 1.

3.1 | Eastern Cooperative Oncology Group Performance Status

PS is used to evaluate functionality, self-care capacity, and the ability to perform daily activities in patients. PS assessment is a determinative independent factor in the prognosis of HNCs, which makes it critical in the decision-making process of treatment.[20] Generally, chemotherapy is contraindicated in patients with ECOG PS > 2 (ambulatory, able to do self-care but unable to carry out any work activities; up and about for >50% of waking hours).[21] Liu et al.[22] stated that an ECOG PS > 1 is significantly and independently associated with shorter overall survival (OS) with an HR of 2.64 compared to patients with ECOG PS ≤ 1.

Our panel reached that an ECOG PS > 2 is considered an absolute contraindication for receiving cisplatin, while an ECOG PS of 2 is relatively contraindicated, that is, puts patients at a high risk along with poor tolerance. This recommendation was consistent with that of the Brazilian panel of experts; however, they added that cisplatin can be indicated in patients with ECOG PS of 2 if the reason

TABLE 1 Summary of panel recommendations pertaining to high-dose cisplatin (100 mg/m^2 every 3 weeks) in HNSCC

Point of Discussion	Absolute Contraindication -1-	Relative Contraindication -2-	Strength of Panel Agreement					
			Strong 90-100%		Intermediate 75%-90%		Weak <75%	
			1	2	1	2	1	2
ECOG PS*	ECOG PS of > 2	ECOG PS = 2	■	■				
Age		≥ 70 years		■				
CCR†	< 50 ml/min	50-60 ml/min	■			■		
Neuropathy	grade ≥ 2	grade = 1	■			■		
Pre-existing hearing loss or tinnitus	grade ≥ 2	grade = 1			■	■		
Baseline involuntary weight loss		≥ 20%				■		
Hepatic impairment		Child-Pugh score B & C		■				
Hematology	Platelets < 100,000/mm^3, neutrophils < 1,500/mm, and hemoglobin < 9 g/dL				■			
Socioeconomic status		Low socioeconomic status				■		
Previous platinum-based chemotherapy		Previous platinum-based chemotherapy				■		
CHF‡	NYHA§ class III or IV	NYHA class I or II CHF + LVEF¶ of ≤ 50%	■	■				

Recommendations:

1. Cisplatin is absolutely contraindicated in patients with ECOG PS > 2 (strong agreement).
2. Cisplatin is relatively contraindicated in patients with ECPG PS of 2 (strong agreement).
3. Cisplatin is relatively contraindicated in patients aged ≥ 70 years (strong agreement).
4. Cisplatin is absolutely contraindicated in patients with CCR < 50 mL/min. (strong agreement).
5. Cisplatin is relatively contraindicated in patients with CCR between 50 and 60 mL/min. (intermediate agreement)
6. Cisplatin is absolutely contraindicated in patients with neuropathy grade ≥ 2 (strong agreement)
7. Cisplatin is relatively contraindicated in patients with neuropathy grade 1 (intermediate agreement)
8. Cisplatin is absolutely contraindicated in patients with pre-existing hearing loss or tinnitus grade ≥ 2 (intermediate agreement).
9. Cisplatin is relatively contraindicated in patients with pre-existing hearing loss or tinnitus grade 1 (intermediate agreement).
10. Cisplatin is relatively contraindicated in patients with involuntary weight loss ≥ 20% (intermediate agreement).
11. Cisplatin is relatively contraindicated in patients with hepatic impairment (Child-Pugh scores B & C) (strong agreement).
12. Cisplatin is absolutely contraindicated in patients with hematological problems (platelets < 100,000/mm3, neutrophils < 1,500/mm3, or hemoglobin < 9 g/dL) (intermediate agreement).
13. The socioeconomic status of patients should be taken into consideration when determining whether patients should be treated with high-dose cisplatin or not (intermediate agreement)
14. Cisplatin is relatively contraindicated in patients who have previously received platinum-based induction chemotherapy (intermediate agreement).
15. Cisplatin is absolutely contraindicated in patients with CHF of NYHA classes III or IV (strong agreement).
16. Cisplatin is relatively contraindicated in patients with CHF of NYHA classes I or II with LVEF ≤ 50% (strong agreement).

Note: All recommendations apply to high-dose cisplatin (100 mg/m^2 every 3 weeks)

Abbreviations: CCR, creatinine clearance; CHF, congestive heart failure; ECOG PS, Eastern Cooperative Oncology Group Performance Status; HNSCC, head and neck squamous cell carcinoma; LVEF, left ventricular ejection fraction; NYHA, New York Heart Association.

behind the poor PS is directly related to the malignancy itself or can be controlled by blood transfusions or treatment of infections.[16]

In 2016, Ahn et al.[17] came out with a conclusion regarding the ECOG PS score through a large expert opinion conducted in the Asia-Pacific region which was also consistent with the decisions of our panel and the Brazilian panel; an ECOG PS of 2 puts patients at high risk for acquiring toxicities, while patients with ECOG PS ≥ 3 are better managed through supportive care measures only.

Also, one member of our panel recommended cetuximab as a safe alternative option for patients of ECOG PS ≥ 2 and this was also suggested in the 2021 NCCN guidelines of HNCs.[14]

3.2 | Age

Our panel recommended that patients aged ≥70 years are relatively contraindicated to receive cisplatin. This recommendation is consistent with that of the Brazilian panel.[16]

Although cisplatin is not absolutely contraindicated in old age, it should still be given with caution given its high complication rates.[16] In 2018, Noor et al.[23] conducted a contemporary review addressing frailty in geriatric patients and the importance of including such factors when individualizing risk assessments and treatment plans in geriatrics.

In the expert opinion by Ahn et al.,[17] biological age rather than calendar age was used in determining relative contraindications to cisplatin through geriatric assessment, as biological age reflects a much clearer health status than calendar age.[17]

In a retrospective study by Chang et al.,[24] a comparison between HNCs patients older and younger than 65 years, who were on CRT from 2007 to 2009 was made. Interestingly, similar clinical characteristics and treatment toxicities were found between the two groups; nevertheless, patients >65 years were less tolerant to cisplatin in terms of having more involuntary weight loss along with hematological toxicities grade > 3, which also concludes the importance of geriatric assessment in elderly patients.[24]

3.3 | Nephrotoxicity

Our panel recommended that cisplatin is absolutely contraindicated in patients with creatinine clearance (CCR) < 50 ml/min, while it is relatively contraindicated in patients with CCR between 50 and 60 ml/min. They also advised about the consideration of preventive measures through regular assessment of glomerular filtration rate and the proper adjustment of cisplatin dose accordingly.

Likewise, the Brazilian panel recommendations by De Castro et al. were absolute and relative contraindications of cisplatin in patients with CCR of <50 ml/min and between 50 and 60 ml/min, respectively. Additionally, the Brazilian panel recommended that predisposing clinical signs and conditions affecting renal function should be closely monitored and fixated, for example, electrolytes, nephrotoxic medications, diabetes mellitus, hypertension, and polycystic kidney disorders.[16]

Ahn et al.[17] added that a CCR < 60 ml/min is considered compromised renal function and recommended cisplatin dose reduction by 50% in patients with CCR between 40 and 60 ml/min. For patients with CCR < 40 ml/min, cisplatin was absolutely contraindicated.

In a retrospective study that analyzed common toxicities behind cisplatin discontinuation, Weykamp et al.[25] found that acute kidney injury was the most commonly reported toxicity (26.7%) that led to cisplatin discontinuation and was predominant in patients aged >60 years.

In a systematic review addressing strategies to prevent cisplatin-induced nephrotoxicity by Crona et al.,[26] hydration with either magnesium supplementation or mannitol (forced diuresis) was found to contribute to a safer use of cisplatin.

3.4 | Neurotoxicity

Cisplatin-induced neurotoxicity initiates as paresthesia and numbness, while it manifests as loss of vibration sense, ataxia, and paresthesia in later cisplatin cycles. Neurotoxicity is considered the most common dose-limiting problem associated with modern cisplatin therapy.[27]

The WHO Neuropathy rating scale involves Grade 0 (no neuropathy symptoms), Grade 1 (paresthesia and/or decrease tendon reflexes), Grade 2 (severe paresthesia and/or mild weakness), Grade 3 (intolerable paresthesia and/or marked motor loss), and Grade 4 (paralysis).[28]

Our panel recommended that patients of neuropathy grade ≥ 2 are absolutely contraindicated to receive high-dose cisplatin, while patients having grade 1 neuropathy are relatively contraindicated.

de Castro et al.[16] considered symptomatic peripheral neuropathy an absolute contraindication to cisplatin and also recommended peripheral neuropathy baseline assessment. Ahn et al.[17] stated that grade 1 neuropathy is relatively contraindicated, and Grade ≥ 2 is absolutely contraindicated with cisplatin indication—and this is consistent with our panel's recommendations.

In a review by Porceddu et al.[29] discussing CRT acute toxicities in HNCs, it was found that neurotoxicity is irreversible when it arises from peripheral nerve damage in 30%–50% of the cases. Neuroprotective drugs were suggested to control cisplatin-induced neurotoxicity, for example, glutathione, vitamin E, and anticonvulsant drugs (such as gabapentin); however, they have not been of evidence yet.[29]

3.5 | Ototoxicity

Cisplatin-induced ototoxicity is a double-factorial process that includes the cisplatin mechanism of action along with the nature of cochlear hair cells. The antineoplastic effect of cisplatin arises from forming intra- and interstrand crosslinks in the DNA after generating monoadducts at guanine or adenine nucleophilic sites; consequently, activation of cell apoptosis by such crosslinks throughout the mitochondrial pathway occurs. Additionally, inner ear damage results from cisplatin uptake into cochlear fluids and hair cells from stria vascularis after being trafficked into the blood–endolymph barrier, from which they enter hair cells. Cisplatin-induced ototoxicity usually appears in terms of either hearing

loss, tinnitus, or vertigo and tends to be permanent despite improvement measures (which is elucidated by the cells' ability to retain cisplatin even after treatment finalization).[30]

Our panel agreed on the high risk (or relative contraindication) of cisplatin indication to patients with grade 1 hearing loss and the absolute contraindication of cisplatin in patients with pre-existing hearing loss or tinnitus ≥ 2, and this is consistent with the recommendations of Ahn et al.[17]

In a 2017 systematic review explicating the differences between cisplatin toxicities in postoperative and definitive settings, ototoxicity represented 2% and 3% of toxicities in the postoperative and definitive settings, respectively.[31] Accordingly, Szturz et al.[32] modified grade 2 hearing impairment from being an absolute contraindication (as per Ahn et al.[17]) to a relative contraindication as long as audiometry checks are done throughout treatment cycles.

The Brazilian panel recommendations were also consistent with ours: baseline hearing loss ≥ 2 is an absolute contraindication to cisplatin. They also shed light on baseline audiogram assessment before treatment for better management of cisplatin-induced ototoxicity.[16] According to the American Academy of Audiology position statement and clinical practice guidelines regarding ototoxicity monitoring, baseline audiology assessment is recommended within 1 week before the initial platinum-based chemotherapy cycle, along with follow-up assessments 24 h before each cycle later on.[33]

Therefore, our panel came out with a conclusion of the necessity of having a multidisciplinary team comprising an audiologist, an oncologist, a clinical pharmacist, and nurses to manage audiometry problems along with considering contributing factors to cisplatin-induced ototoxicity—which include dose, concomitant RT, renal insufficiency, nutritional deficiency, genetic factors, age, and pre-existing hearing impairment.

3.6 | Weight loss

Cisplatin-induced weight loss is claimed to be independent of dose and of more association with treatment frequency. Upon comparing cisplatin weekly and 3-weekly approaches along with correlating with induced toxicities, Colevas et al.[31] found that the weekly cisplatin approach significantly induced more dysphagia (Grade 3–4) and weight loss than the 3-weekly approach.[31]

Our panel recommended that cisplatin is relatively contraindicated in patients with involuntary weight loss ≥20%. Likewise, the Brazilian panel came out with the same recommendation of having such a percentage of weight loss as a relative contraindication along with pointing out the nutritional consultation necessity for these patients.[16] Ahn et al.[17] also considered weight loss ≥20% a serious and dose-limiting side effect that requires attention and early management as well.

Individualized nutritional counseling along with oral nutritional supplements are important in controlling chemotherapy/radiation-induced weight loss, owing to the fact that statistically significantly less worsening in weight and nutritional status was found after applying a case-based nutritional consultation rather than the basic nutritional counseling.[34]

3.7 | Hepatic impairment

Given the fact that viral hepatitis is considered one of the most public health challenges in Egypt, monitoring cisplatin-induced hepatotoxicity is crucial especially in patients with concomitant hepatitis B virus (HPV).[35] Baseline hepatic function assessment was suggested to avoid interrupting therapy as a result of hepatic intolerance to cisplatin high doses. Our panel also agreed that cisplatin is relatively contraindicated in patients with hepatic impairment (Child–Pugh Scores B and C).

While in the Brazilian panel, Child–Pugh scores of either B or C were considered an absolute contraindication, unless adequate treatment of viral hepatitis (antiviral) is concurrently given and can be maintained till the end of cisplatin treatment.[16] Ahn et al.[17] stated that patients with Child–Pugh Score B receiving cisplatin are at high risk, and Szturz et al.[32] added the absolute contraindication to cisplatin in patients with Child-Pugh score C.

3.8 | Hematological toxicities

The prevalence of leukopenia and neutropenia in the 3-weekly high-dose cisplatin setting is significantly higher than the weekly low-dose.[31] Our panel recommended that patients with hematological problems in terms of platelets < 100,000/mm^3, neutrophils < 1500/mm^3, or hemoglobin < 9 g/dl are absolutely contraindicated to receive cisplatin, and this is consistent with the Brazilian panel recommendations.[16]

3.9 | Socioeconomic status

In 2006, Vartanian et al.[36] assessed the effect of socioeconomic factors on HNC patients; out of 301 enrolled patients, 32% showed work-related disability. Hence, attention should be given to such factors, especially in households where patients are the main contributors to the income of the house.[36]

Our panel indicated that the socioeconomic status of patients should be taken into consideration when determining whether patients should be treated with high-dose cisplatin or not. Also, Ahn et al.[17] stated that impaired socioeconomic support is a relative contraindication to receiving cisplatin. Szturz et al.[32] also came out with the same conclusion.

3.10 | Previous platinum therapy (induction chemotherapy)

Our panel agreed that patients who were previously given induction chemotherapy (ICT) and are currently receiving cisplatin are at high risk due to the potentiality of high-risk cumulative toxicity along with poor compliance. This is compatible with Ahn et al.[17] Also, the NCCN highlighted that ICT followed by a high dose 3-weekly cisplatin is accompanied by toxicity concerns.[14] Hence, adequate management of post-ICT adverse events is critical.

Additionally, in a randomized phase III trial by Ghi et al.[37] assessing OS, complete response (CR), progression-free survival (PFS), and LRC between ICT and no-ICT, results were found to be significantly better in the ICT arm (median OS = 54.7 vs. 31.7 months, median PFS = 30.5 vs. 18.5 months, CR = 42.5% vs. 28%, and LRC = 41% vs. 48%, in the ICT and no-ICT arms, respectively). Hence, ICT use is encouraged but with keeping caution during subsequent treatment.[37] In another prospective phase II study conducted in China on patients with unresectable HNSCC, the response rate after ICT was 89%, which also supports ICT use.[38]

3.11 | Cardiotoxicity

Our panel agreed on the absolute contraindication of cisplatin in patients with New York Heart Association (NYHA) Class III or IV CHF even if cardiovascular (CV) therapy is optimized. They also agreed on the relative contraindication of cisplatin in NYHA Class I or II with left ventricular ejection fraction ≤ 50%. This is congruent with the Brazilian panel as well, in addition to the fact that cisplatin is correlated with arterial events that require caution with high cisplatin doses.[16] Ahn et al.[17] considered patients with CV diseases including hypertension or unstable cardiac disease and receiving cisplatin at high risk.

Cisplatin does not usually induce cardiotoxicity; nonetheless, cardiotoxic events following cisplatin treatment have become recurrent and can be extended to CHF. The life-threatening risk of cisplatin-induced cardiotoxicities arises from them being sometimes silent, especially arrhythmias. Cardiotoxic mechanisms occur as a result of either cisplatin-induced cardiotoxicity itself or indirectly through nephrotoxicity. Also, electrolyte imbalance especially hypomagnesemia (serum levels less than 1.7 mg/dl) is considered a major contributing factor to cisplatin-induced cardiotoxicities. According to Liu et al.,[22] the frequency of hypomagnesemia is also significantly associated with shorter OS. Given that intracellular concentrations of magnesium are hard to measure along with its criticality in predisposing patients to such silent lethal toxicities, cardiac monitoring should be indispensable during cisplatin infusion.[39]

Last but not least, despite the fact that cisplatin induces a wide range of toxicities, it still remains the mainstay treatment option in HNCs. Cisplatin-ineligible patients can receive cetuximab or carboplatin instead. In a retrospective study by Hamauchi et al.[40] investigating the safety and efficacy of either carboplatin or cetuximab in cisplatin-ineligible patients, LRC rates were 56% and 58%, and median PFS durations were 42.7 and 11.6 months for carboplatin and cetuximab, respectively. Nevertheless, grade III/IV hematological toxicities were found with carboplatin, while cetuximab was associated with grade III/IV mucositis. Consequently, they can be used as an alternative option to cisplatin, yet alertness to toxicities is still mandatory.[40]

4 | CONCLUSION

Our panel discussion established a set of evidence-based recommendations for cisplatin eligibility criteria in patients of HNSCC in Egypt.

AUTHOR CONTRIBUTIONS

Mohamed Abdulla: Conceptualization; methodology; writing – review and editing. **Abdel Aziz Belal**: Conceptualization; methodology; writing – review and editing. **Amr Sakr**: Methodology; writing – original draft; writing – review and editing. **Lobna E. El Arab**: Data curation; formal analysis; writing – review and editing. **Mohsen Mokhtar**: Formal analysis; methodology; writing – review and editing. **Nasr Allahloubi**: Conceptualization; methodology; writing – review and editing. **Ramy Ghali**: Conceptualization; methodology; writing – review and editing. **Tarek Hashem**: Conceptualization; methodology; writing – review and editing. **Waleed Arafat**: Conceptualization; methodology; writing – review and editing. All authors have read and approved the final manuscript.

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CONFLICT OF INTEREST

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DATA AVAILABILITY STATEMENT

The datasets used and/or analyzed during the current study are available from the corresponding author upon reasonable request. Mohamed Abdulla had full access to all of the data in this study and takes complete responsibility for the integrity of the data and the accuracy of the data analysis.

TRANSPARENCY STATEMENT

The lead author Mohamed Abdulla affirms that this manuscript is an honest, accurate, and transparent account of the study being reported; that no important aspects of the study have been omitted; and that any discrepancies from the study as planned (and, if relevant, registered) have been explained.

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