Chapter 19
New Developments in Surgery for Malignant Salivary Gland Tumors

J. Meulemans, C. Van Lierde, P. Delaere, J. J. Vranckx, and V. Vander Poorten

Introduction

Salivary gland carcinomas (SGC), arising either from the major salivary glands (MaSGC) or the minor salivary glands (MiSGC), are rare entities comprising many different histologies with variable biological behavior. The surgical management of SGC is challenging, due to the often close proximity of the tumor to important anatomic structures such as the facial, lingual and hypoglossal nerves and adjoining vascular and musculoskeletal structures and due to the anatomic complexity of the regions involved, such as the nasopharynx and the skull base in case of MiSGMT's [1]. Given its rarity, its variety in histologic subtypes, its broad spectrum of involved anatomic locations and in addition, outcome studies which often have a retrospective design with a heterogeneous patient population, the optimal management of SGS has remained subject to controversy. However, there is agreement on following principles of treatment. First, primary surgery with achievement of clear surgical margins, followed by adjuvant radiotherapy as indicated based on the definitive pathological assessment of the surgical specimen, is commonly regarded as the primary treatment of choice for SGC [1–3]. Second, a rigorous pre-surgical work-up and appropriate planning of surgery and radiotherapy contribute to the success of treatment [1–3]. Third, the treatment needs to be tailored to the tumor and the patient, in order to minimize treatment-related morbidity and maximize postoperative function preservation,

J. Meulemans · C. Van Lierde · P. Delaere · V. Vander Poorten (✉)
Otorhinolaryngology-Head and Neck Surgery, University Hospitals Leuven, Herestraat, 49 3000 Leuven, Belgium
e-mail: vincent.vanderpoorten@uzleuven.be

J. Meulemans · C. Van Lierde · V. Vander Poorten
Department of Oncology, Section Head and Neck Oncology, KU Leuven, Leuven, Belgium

J. J. Vranckx
Department of Plastic & Reconstructive Surgery, KU Leuven University Hospitals, Leuven, Belgium

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recovery and rehabilitation [1–3]. In recent years, interesting developments in ablative and reconstructive surgical procedures have emerged. They focus on reducing postoperative morbidity while maximizing function preservation, often via minimally invasive approaches (transoral laser or robotic surgery, transnasal endoscopic surgery etc.) on the one hand, and on optimization of the anatomic and functional reconstruction after tumor ablation on the other hand, leading to more rapid function rehabilitation and better esthetic outcomes.

Developments in Ablative Surgery

Transoral Surgery: TLM and TORS

Transoral endoscopic head and neck surgery, including both transoral laser microsurgery (TLM) and transoral robotic surgery (TORS), provides a means of accessing a range of anatomic sites in the upper aerodigestive tract that have traditionally been difficult to approach, such as the oropharynx, the supraglottic larynx and the hypopharynx. Additional advantages of TORS over TLM are enhanced visualization with 3-dimensional vision and tenfold magnification, elimination of physiological tremor leading to more surgical precision and restoration of proper hand–eye coordination. Furthermore, the use of multi-articulated instruments with 7 degrees of freedom improves dexterity and maneuverability, and as a result, overcomes the limits of the line-of-sight issue and typical tangential-only cutting plane as encountered in TLM. All this results in accessability in a selection of tumors, which are unapproachable by TLM [4, 5]. Whereas TLM and TORS have a proven track record in the primary surgical treatment of selected squamous cell carcinomas (SCC), with evidence being most abundant for treatment of laryngeal SCC by TLM and oropharyngeal SCC by TORS, only few reports have been published on transoral resection of MiSGC arising in the upper aerodigestive tract (oropharynx, larynx) [6–11]. The rationale for using transoral surgery is that it is a minimally invasive 'natural orifice' surgery that, compared to the classic transcervical and transmandibular approaches, dramatically reduces interference with healthy surrounding tissues thus resulting in less postoperative morbidity, less pain, faster recovery, shorter hospitalization and better functional outcomes. These advantages have been illustrated in comparative studies on open approaches versus TORS for oropharyngeal SCC (OPSCC), both in the primary and salvage settings [12, 13].

As a substantial part of the MiSGC arise in the oropharynx, with the base of tongue (BOT) being the most commonly affected subsite (78% of oropharyngeal MiSGC), classical TORS procedures such as radical tonsillectomy/lateral oropharyngectomy and BOT resection have been applied to MiSGC [14, 15]. Feasibility and safety of TORS for management of oropharyngeal MiSGCs was first illustrated by Villanueva et al. in 2013 in 10 patients with either T1 or T2 tumors. Free surgical margins were achieved in all cases, locoregional control after 2 years was 80% and functional outcomes proved excellent with mean postoperative MD Anderson Dysphagia Index (MDADI) scores of 99/100. However, postoperative functionality was only measured in 6 patients at a random time point [16]. Schoppy and colleagues reported on 20 patients with MiSGCs of the oropharynx managed with endoscopic approaches, either TORS or TLM. Adenoid cystic carcinoma (AdCC) was the most common histology, accounting for 35% of cases and the BOT was the most commonly affected subsite (75%). Of the 20 patients included in the analysis, 10 underwent TORS followed by adjuvant radiation therapy. Postoperative complications were limited, with one patient (5%) returning to the operating theatre for control of post-operative oropharyngeal bleeding; no long-term tubefeeding or tracheotomy dependency were reported. On an average follow-up of 36 months, 90% of patients were alive with no evidence of recurrence [17].

In a recent retrospective analysis of the National Cancer Database (NCDB), perioperative outcomes and overall survival of patients with oropharyngeal MiSGC treated with TORS were compared to outcomes of patients treated by other approaches. In a total of 785 analyzed patients, no significant differences in positive margin rate, 30-day mortality or overall survival between groups were reported. Although the 30-day unplanned hospital readmission rate was higher in patients treated with TORS versus non-robotic resections (5.8 vs. 1.7%, $p = 0.0004$), when stratified by tumor subsite, there was a significant decrease in hospital length of stay in patients with BOT SGCs treated with TORS versus non-robotic resections ($p = 0.029$) [14]. Although current evidence is limited to retrospective studies reporting on outcomes of small patient populations with short follow-up, the abovementioned data suggest that transoral endoscopic head and neck surgery may be considered a valuable treatment modality in the multidisciplinary management of MiSGCs (Fig. 19.1) [18].

Additionally, TORS has recently been attempted for primary parapharyngeal space tumors, which often derive from the deep lobe of the parotid and present as a mass in the prestyloid compartment of the parapharyngeal space (PPS). Traditionally, these tumors are addressed by a transcervical, transparotid or transmandibular approach, as the classic, non-robot assisted transoral approach offers limited exposure to the PPS, with lack of control of the great vessels and cranial nerves and hence, possibility of neurovascular injury [19]. These limits can be overcome by TORS, offering better visualization and more precision compared to the conventional transoral approach. TORS candidates are patients with adequate exposure of the oropharynx and whose preoperative assessment reveals a well-circumscribed neoplasm with lateral displacement of the internal carotid artery and clear cleavage plane from the neurovascular bundle [19]. TORS may be used in both pre- and retrostyloid tumors, however, the far lateral and superior areas of the PPS are inaccessible by this technique and require transcervical assistance [20]. Although several case series and reviews confirmed safety and feasibility of TORS for selected PPS tumors, this needs to be interpreted with caution as only a small minority of PPS tumors treated with TORS were malignant [20–22]. Moreover, TORS for PPS lesions has some drawbacks such as the high rate of capsula rupture with resulting tumor fragmentation and spillage, lack of carotid artery protection and need for division of

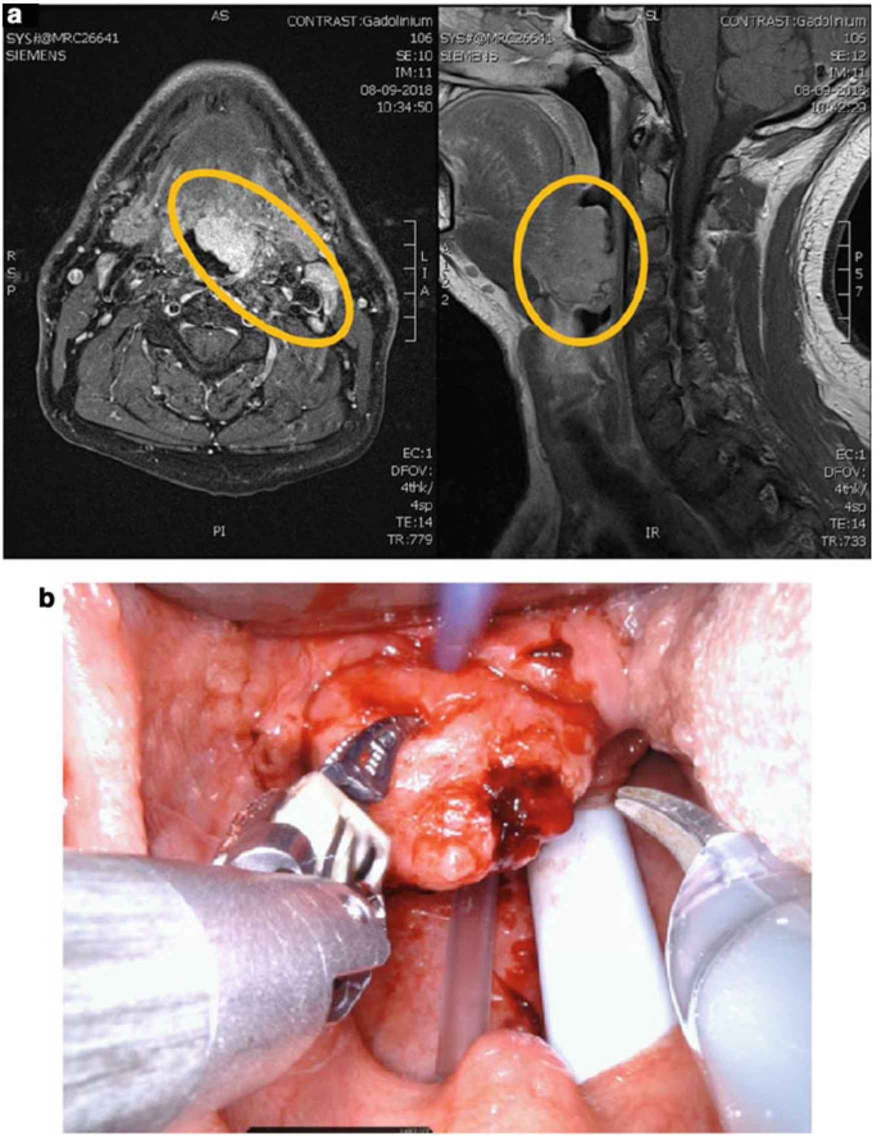

Fig. 19.1 Hyalinizing clear cell carcinoma (HCCC) of left base of the tongue. **a** Gadolinium-enhanced magnetic resonance imaging of clinical stage cT3N1 HCCC. The left panel shows the primary tumor and a level II lymphadenopathy on axial images. The right panel shows a sagittal T1-weighted image of the base of tongue tumor filling the vallecula and pushing the epiglottis down. Yellow circles show the tumor infiltration. **b** Transoral robotic resection and ipsilateral comprehensive neck dissection resulted in a pathologic stage pT3N2b HCCC. This figure was previously published elsewhere and approved for reproduction (18)

the parapharyngeal mucosa and superior constrictor muscle which is associated with considerable postoperative pain. Moreover, no comparative data of postoperative speech, swallowing and pain outcomes of TORS versus the transcervical approach exist. As such, there is currently no conclusive evidence that this approach is truly ‘minimally invasive’ [22]. Together with the lack of large case series and sound oncological outcome data, TORS for malignant PPS tumors should be considered only in very selected cases and should be performed by very experienced robotic surgeons, given the anatomic complexity of the PPS.

Finally, some technical developments related to the current robotic platforms, which have a suboptimal design for TORS, may optimize the capability of TORS for treating malignant salivary gland tumors arising in the upper aerodigestive tract. Monopolar electrocautery, the most common dissection and coagulation tool during TORS causes significant collateral tissue damage; the latter is far less common when using a CO_2 laser as a cutting device. As such, implementation of CO_2-laser technology during TORS could be of substantial benefit. In a recently published study, feasibility and safety of a newly developed steerable CO_2-laser fiber carrier compatible with the existing Endowrist® monopolar spatula of the Da Vinci Xi (Intuitive Inc, Sunnyvale, CA, USA) were illustrated in a preclinical setting, with the prototype successfully combining advantages of CO_2-laser with advantages of TORS [23].

Transnasal Endoscopic Surgery

For selected naso-ethmoidal MiSGMTs, especially AdCC of the ethmoid, small case series have supported the use of endoscopic transnasal surgery [1]. In a retrospective case series including 34 patients affected by sinonasal AdCC treated by an endoscopic endonasal approach, the authors report excellent oncological outcomes with 5-year disease-specific survival and recurrence-free survival rates of 86.5% and 71.8% respectively [24]. Similarly, it has been shown that MiSGCs localized in the nasopharynx without involvement of the internal carotid artery and minimal extension to the skull base can be effectively managed with transnasal endoscopic surgery [1].

For MiSGCs arising in the upper jaw, requiring maxillectomy, endoscopic approaches are also increasingly used in combination with and preceding standard external maxillectomy techniques. Before the en bloc resection, the retromaxillary and infratemporal tumoral extension is controlled endoscopically and the pterygomaxillary junction is drilled to allow for a more precise and safer way to perform the posterior osteotomy. This combination of both open and endoscopic techniques optimizes the radicality of resection through better exposure of the medial and posterior extent of the lesion and by more precise delineation of the surgical margins, in particular the most difficult posterior margin (Fig. 19.2). This is illustrated by the high rates of clear margins posteriorly (96%) and the low incidence of local recurrence posteriorly (5.3%) as reported by Deganello et al. in a retrospective review of 79 patients who underwent endoscopic-assisted maxillectomy for nasoethmoidal,

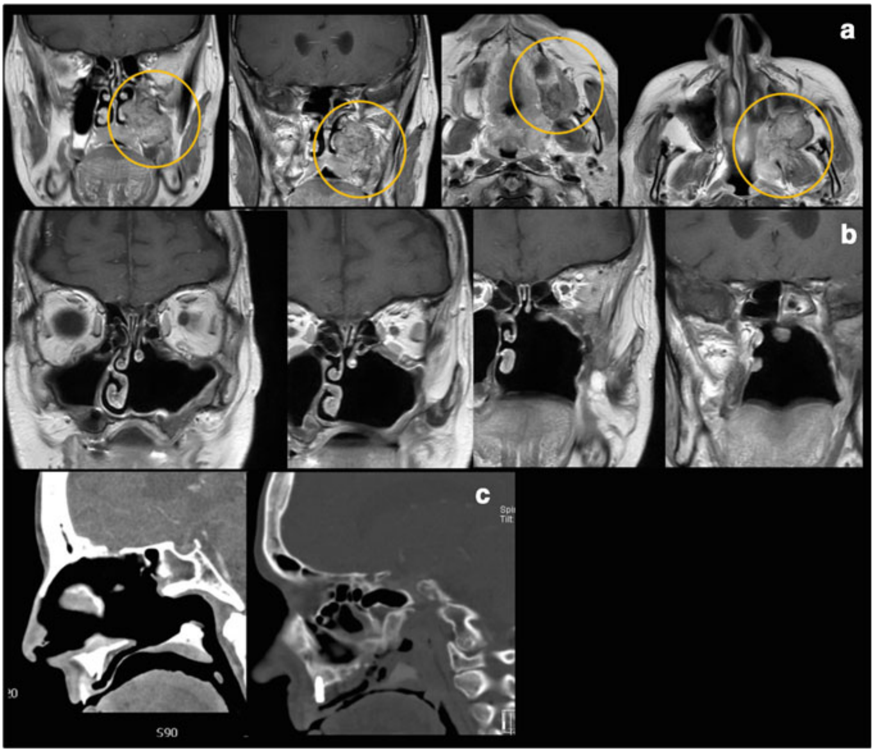

Fig. 19.2 **a** T1-weighted MRI of a T3N0 myoepithelial carcinoma ex pleomorphic adenoma of the left pterygopalatine fossa. **b** Postoperative MR showing the status after combined endoscopic—transoral resection. **c** CT scan showing implant retained obturator with good speech and swallowing function. Following postoperative image-guided radiotherapy (IMRT) to 66 Gy, the patient is now 3 years free of disease

maxillary, or hard palate cancer with a substantial portion of patients being affected by MiSGCs (17/79 or 21.5%) [25].

Developments in Reconstructive Surgery

Regarding recent evolutions in reconstructive surgery, mainly new developments in reconstruction following radical parotidectomy have emerged. The immediate reconstruction of the face in the setting of radical parotidectomy for malignancy represents a particular challenge because of the complexity of the defect, the frequent need for postoperative radiotherapy, the often advanced patient age, and possible limited life expectancy [1, 26].

Developments in Midface Reanimation

Common approaches to midface reanimation are the use of static slings, temporalis myoplasty and innervated free muscle transfers (most often the gracilis muscle). The eye is commonly protected through lid loading and lateral tarsorraphy or canthoplasty. Additionally, fasciocutaneous flaps (e.g., anterolateral thigh (ALT) flap) are routinely used for skin and soft tissue replacement, while reconstruction of the facial nerve is commonly performed with free nerve cable grafting. However, given the advanced age of most patients and the likelihood of postoperative radiotherapy, the recovery of spontaneous movement through free nerve grafting is slow, unpredictable and often suboptimal [27]. Moreover, development of troublesome synkinesis by misdirecting regenerating axons and simultaneous activation of multiple muscle groups frequently occurs [1].

When compared to free nerve grafts, the use of vascularized nerve grafts (VNGs), such as the radial forearm flap (RFF) with dorsal sensory branches of the radial nerve (DSBRN) and ALT with the lateral femoral cutaneous nerve (LFCN) or deep motor branch of the femoral nerve to vastus lateralis (DMBVL), are claimed to improve functional facial recovery outcomes, when compared to free nerve grafts [28]. In a retrospective review of 12 patients who underwent radical parotidectomy and immediate facial nerve reconstruction with VNGs, 8 patients (75%) regained at least resting symmetry [28]. The use of vascularized nerve grafts implies microvascular anastomosis and the donor nerve grafts are harvested together with adipofascial tissue to maintain nerve vascularity. As an additional advantage, the associated adipofascial component of these flaps (e.g., deepithelialized RFF) helps augment the soft tissue contour defect after tumor ablation. Hence, only 1 donor site is required to reconstruct both the contour and neuromuscular deficits. This contrasts with free nerve grafts, which are typically harvested from sites remote to the free flap.

Another option for reanimating the paralyzed face after radical parotidectomy, which recently became increasingly popular, is the use of the masseteric nerve, a motor branch of the mandibular nerve, for reinnervation of the midface and lip musculature (Fig. 19.3). Its position within the subzygomatic triangle and thus close proximity to the buccal branch of the facial nerve allows a tension-free coaptation without the need for cable grafting, which translates into a faster recovery of function; the regenerating axons have only a short distance to travel to reach the fascial muscles. Moreover, the masseteric nerve has a significantly higher axonal count as compared to the proximal stump of the facial nerve, which adds to the swift return of neural function which can be seen as early as 2 months postoperatively [29]. As a consequence of this high axonal density of the masseteric nerve, the masseter to buccal branch transfer (MBBT) produces strong oral commissure excursion with clenching, but lacks the spontaneity and resting tone achieved with interposition nerve grafting between the main trunk of the facial nerve and its distal branch(es). Given this consideration, several authors propagate a dual innervation approach in which a MBBT is combined with proximal facial nerve grafting to the remaining distal branches (which is only possible if the main trunk of the facial nerve could be

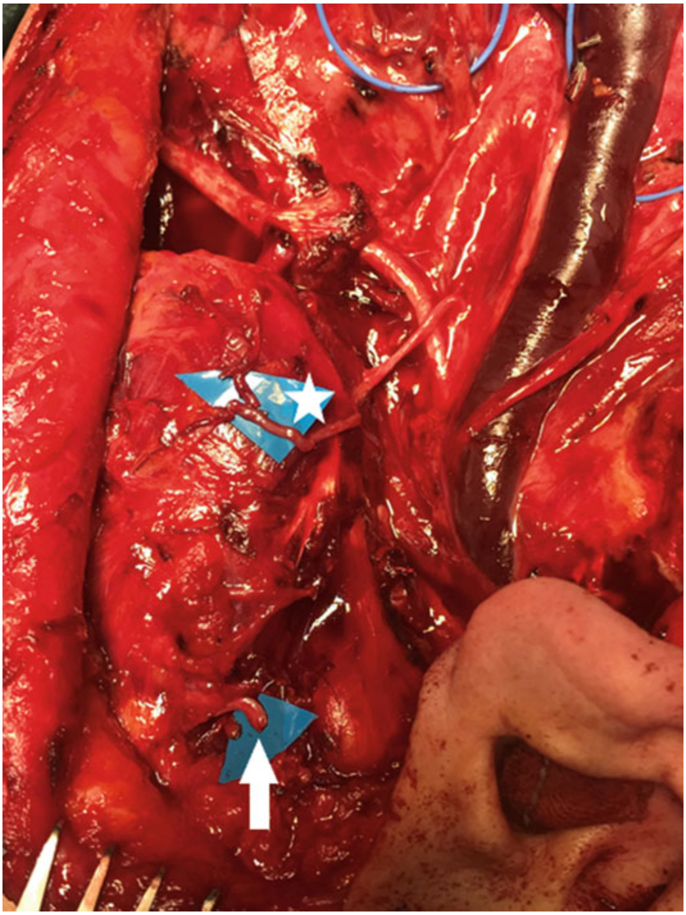

Fig. 19.3 Radical parotidectomy defect with sacrifice of the main trunk of the facial nerve. The masseteric nerve and the buccal branch of the facial nerve are identified and prepared for a masseter to buccal branch transfer (MBBT) (white arrow). The descending hypoglossal branch of the ansa cervicalis is reflected cranially and prepared for neural coaptation with the marginal branch of the facial nerve (white star)

spared during the ablative procedure), resulting in a more reliable but still voluntary smile [26, 29]. Moreover, this combined approach decreases the troublesome synkinesis by providing 2 separate nerve inputs to different facial muscle groups: the cable grafting restores tone to areas in the lower eyelid and midface whereas the MBBT is targeted to the lower facial muscle group, allowing for independent movement of the oral commissure [29]. It has to be noted that MBBT has minimal morbidity and that MBBT is also possible when the proximal stump of the facial nerve is unavailable due to the extent of the resection [26].

Developments in Single Stage Reconstruction of Complex Defects Using Free Flaps

Recently, new free flaps have been described which are suitable for single stage reconstruction of complex defects after radical parotidectomy. These include the ALT with dual chimeric innervated vastus lateralis free flap which is suitable for both cutaneous reconstruction and dynamic reanimation of the midface after radical parotidectomy with resection of the peripheral facial nerve branches. In this single stage reconstructive approach, 2 muscle units of the vastus lateralis muscle on separate nerves are harvested in combination with the ALT fasciocutaneous flap on a single vascular pedicle, creating a chimeric flap. The larger muscle unit is inserted directly to the oral commissure to suspend the midface and an end-to-end neural coaptation between the nerve to the vastus muscle and the masseteric nerve is performed. The smaller muscle unit is inserted into the upper eyelid to assist eye closure, followed by neural coaptation to the upper division of the facial nerve when available, or to the facial nerve stump. Due to the dense aponeurosis, the vastus lateralis muscle units provide a reliable static suspension until reinnervation kicks in. The ALT fasciocutaneous flap is used to restore the cutaneous defect or deepithelialized for contour restoration when no skin is required [27].

Another new flap described for single stage reconstruction of radical parotidectomy defects is the thoracodorsal artery perforator and nerve flap (TAPN) flap, which allows for skin or soft tissue reconstruction in combination with facial nerve reconstruction from the trunk of the facial nerve to 4–6 distal facial nerve branches [30, 31]. This flap can be designed according to the defect and the soft tissue required, including either an adipocutaneous paddle or only fat tissue if no skin resection was performed. Moreover, the main trunk of the thoracodorsal nerve is elevated together with the thoracodorsal artery and vein, in order to preserve the vascularization of the thoracodorsal nerve and its distal branches, which can be adapted to the facial nerve defect. As such, the thoracodorsal nerve and its branches are considered VNGs with inherent advantages compared to free nerve grafts (cfr supra) [30].

Conclusion

Although many promising developments in ablative and reconstructive surgical treatment of salivary gland malignant tumors have been reported, the current evidence supporting their added value remains limited. Reports are often small retrospective series that lack rigorous follow-up of both functional and oncological outcomes. As such, future comparative research is necessary in order to identify the most optimal ablative and reconstructive techniques in relation with specific indications, potentially allowing for future evidence-based patient-tailored approaches.

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