Current Status of Clinical Trials in Head and Neck Cancer 2014

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Abstract

Introduction. The last few years have seen significant increase in the number of available clinical trials in head and neck cancer. It has been difficult to stay abreast of these efforts because multiple cooperative groups and institutions are engaged in their recruitment. This review presents the state of the art of available clinical trials organized around major research themes.

Data Sources. Published literature, published cooperative group monographs, expert review.

Review Methods. Initial themes in head and neck cancer clinical trial development were first identified along with examples. Opinions from an international panel of multidisciplinary experts were then solicited.

Results/Discussion. Current major themes of head and neck clinical trials centered on 5 major themes: (1) recognition of human papillomavirus oropharynx cancer and optimal treatment strategies, (2) defining the role of transoral surgery in head and neck cancer treatment, (3) improving postoperative adjuvant treatment, (4) investigation of rare malignancies, and (5) the importance of biomarker-driven, innovative, and targeted therapy investigation.

Conclusions. A number of exciting clinical trials are currently in development or accrual with the potential for tremendous impact and improvement of the treatment of head and neck cancer.

Implications for Practice. Awareness by practicing otolaryngologists and trainees of these current themes will be essential for study accrual, success, and improvement in the care of head and neck cancer.

Keywords

clinical trial, head and neck neoplasms, human papillomavirus, oropharyngeal carcinoma, review

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In recent years, head and neck oncology has seen several significant new developments, including recognition of the implications of human papillomavirus (HPV)–associated oropharynx squamous cell carcinoma (OPSCC); the greater use of transoral surgery for the treatment of head and neck squamous cell carcinoma, primarily driven by robotic surgery; more general application of intensity-modulated radiation therapy; and application of advances in molecular medicine to regimen development and assessment of treatment response. Clinical trials have begun to study these developments in the treatment of head and neck cancer. The focus of this review is current efforts by the National Cancer Institute (NCI) in head and neck cancer.

In North America, government-funded clinical trials have for decades been primarily managed through the cooperative oncology groups. Nine adult cooperative groups have composed the system. Among these groups, the Eastern Cooperative Oncology Group (ECOG), the Radiation Therapy Oncology Group (RTOG), and the American College of...
Surgeons Oncology Group have had active head and neck cancer programs. Recently, the 9 groups have been reorganized into the National Clinical Trials Network, consolidating into 4 major groups for treating adult cancer: Alliance for Clinical Trials in Oncology, ECOG-ACRIN (American College of Radiology Imaging Network), NRG Oncology (National Surgical Adjuvant Breast and Bowel Project, RTOG, and Gynecologic Oncology Group), and SWOG (Southwestern Oncology Group). The American College of Surgeons Oncology Group has now been incorporated into the alliance, while RTOG has been incorporated into NRG Oncology. While both ECOG-ACRIN and NRG Oncology (RTOG) maintain active head and neck cancer committees, future clinical trials will be conducted through the National Clinical Trials Network in an effort to consolidate goals and to expand access.

With the recent consolidation of the cooperative groups and the increasing availability of head and neck clinical trials, it can be difficult to stay abreast of their status. The goal of this review is to summarize current major themes in NCI-funded head and neck cancer clinical trials. The primary intended audience is general otolaryngologists and residents/fellows in training.

Current and developing head and neck clinical trials have addressed the following major research themes:

1. Recognition and description of HPV-associated oropharynx cancer (HPV OPSCC) and identification of optimal treatment strategies for both HPV-positive and HPV-negative disease
2. Defining the role of transoral surgical approaches in the treatment of head and neck cancer, particularly oropharynx cancer
3. Improvement of postoperative adjuvant treatment
4. Investigation of rare malignancies
5. Importance of biomarker-driven, innovative, and targeted therapy investigation

This review of current trials, most either accruing or under development, is not intended to be exhaustive but will highlight efforts in these areas. Trials highlighted include phase IIR and phase III trials. Phase IIR trials are randomized trials whose goal is to evaluate effectiveness and safety in a smaller cohort; actual end points vary by design. Phase III trials are larger randomized trials, usually hundreds of patients, used to confirm observed treatment effectiveness and monitor side effects. They are usually designed following results from phase II trials. Through reviewing these major efforts in head and cancer clinical trials, we hope to impress on the otolaryngology community and trainees the need and benefit of enrolling our patients into such trials and offering them the best care in the process. A summary of studies reviewed in this study is presented in Table 1.

**Methods**

Initial themes in head and neck cancer clinical trial development were first identified by the senior author (D.J.A.). Clinical trials either in development or open to accrual were identified that illustrated these themes and were organized into a draft monograph. Opinions from an international panel of multidisciplinary experts currently involved in head and neck cancer clinical trial development were then solicited to generate a final manuscript.

**Discussion**

**HPV Oropharynx Cancer Treatment**

HPV has been identified as a causative pathogen in OPSCC. HPV-positive oropharynx cancer (HPV OPSCC) is now considered a distinct clinical entity. Patients with HPV OPSCC tend to be younger with a different profile of risk exposure than that of OPSCC caused by substance abuse—primarily alcohol and tobacco. The presence of HPV DNA in these oropharynx cancers is the defining characteristic of these tumors, and p16 overexpression has proven a useful and excellent surrogate for HPV positivity. Most important, HPV OPSCC responds better to treatment than does non-HPV OPSCC and is associated with a significantly improved overall survival, as shown in analysis of 2 major clinical trials (ECOG 2399 and RTOG 0129). With modern treatment, the majority of patients with HPV OPSCC will survive. Current research efforts have focused on defining treatment strategies that are less toxic than standard concomitant chemoradiation with high-dose cisplatin in the treatment of the favorable risk patients with locoregionally advanced HPV OPSCC, as well as on improving outcomes in those poor-risk non-HPV patients.

In 2008, the NCI hosted a meeting of physicians and scientists on head and neck cancer and its association with HPV. Through that meeting, the role of HPV in oropharynx cancer was highlighted and considerations for clinical trial design discussed. RTOG 1016 was one such trial that developed from this meeting. RTOG 1016, which closed to accrual in September 2014, was a phase III trial for HPV OPSCC. Entry criteria were untreated advanced stage HPV- or p16-positive oropharynx cancer. Patients treated with radiation therapy were randomized to receive either concurrent cisplatin or concurrent cetuximab. The primary goal of this study was to determine whether chemoradiation with a presumably less toxic agent (ie, cetuximab) offered the same oncologic outcome as treatment with cisplatin.

NRG-HN002, which is under development, is a phase IIR trial for the best-prognosis patients with HPV OPSCC: nonsmokers with T1-2N1-2b or T3N0-2b tumors. These patients will be randomized to 1 of 2 treatment arms. They will receive either a reduced radiation dose alone with an accelerated fractionation regimen (60 Gy in 5 weeks) or chemoradiation with a reduced dose of radiation with standard fractionation (60 Gy in 6 weeks) and weekly cisplatin. Both arms in this trial will use the lower total radiation dose of 60 Gy rather than the standard 70 Gy. The purpose again is to reduce late toxicity by reducing radiation dose and duration in these very good risk patients, without compromising efficacy. Dose reduction would be considered successful if the 2-year progression-free survival is at least
### Table 1. Clinical Trials Referenced in this Article (as of September 25, 2014).

<table>
<thead>
<tr>
<th>Trial Name</th>
<th>Status</th>
<th>Trial Title</th>
<th>Tumor Type</th>
<th>Primary Objective</th>
<th>Accrual Target</th>
</tr>
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<tbody>
<tr>
<td>RTOG 1016</td>
<td>Closed</td>
<td>Phase III Trial of Radiotherapy Plus Cetuximab Versus Chemoradiotherapy in HPV-Associated Oropharynx Cancer</td>
<td>Squamous cell carcinoma of the oropharynx; stage T1-2, N2a-3 or T3-4, any N; tumor must be p16 positive</td>
<td>To determine whether substitution of cisplatin with cetuximab will result in comparable 5-y overall survival</td>
<td>834</td>
</tr>
<tr>
<td>NRG HN002</td>
<td>Proposed</td>
<td>Phase III Trial for Patients with p16 Positive, Non-Smoking Associated, Locoregionally Advanced Oropharyngeal Cancer</td>
<td>Pathologically proven p16-positive oropharynx cancer, &lt;10 y of smoking, T1-2, N1-2b, T3N0-2b</td>
<td>Randomized trial of accelerated but reduced-dose radiation therapy alone vs reduced-dose radiation therapy and cisplatin; 2-y progression-free survival of 91% despite treatment de-escalation</td>
<td>328</td>
</tr>
<tr>
<td>ECOG 3311</td>
<td>Open</td>
<td>Phase II Randomized Trial of Transoral Surgical Resection followed by Low-dose or Standard-dose IMRT in Resectable p16+ Locally Advanced Oropharynx Cancer</td>
<td>Advanced p16-positive squamous cell carcinoma of the oropharynx.</td>
<td>Determine difference in progression-free survival between low- and standard-dose intensity modulated radiation therapy for p16-positive locoregionally advanced oropharynx cancer.</td>
<td>377</td>
</tr>
<tr>
<td>RTOG 1221</td>
<td>Open</td>
<td>Randomized Phase II Trial of Transoral Endoscopic Head And Neck Surgery followed by Risk-Based IMRT and Weekly Cisplatin versus IMRT and Weekly Cisplatin for HPV Negative Oropharynx Cancer</td>
<td>Squamous cell carcinoma of the oropharynx; stage III-IV; T1-2, N1-2b; not approaching within 1 cm of midline; amenable to transoral resection; tumor must be p16 negative</td>
<td>To determine if primary treatment with transoral endoscopic head and neck surgery will improve progression-free survival for patients with human papillomavirus–negative oropharynx cancer.</td>
<td>144</td>
</tr>
<tr>
<td>RTOG 1216</td>
<td>Open</td>
<td>Randomized Phase II/III Trial of Surgery and Postoperative Radiation Delivered with Concurrent Cisplatin versus Docetaxel versus Docetaxel and Cetuximab for High-Risk Squamous Cell Cancer of the Head and Neck</td>
<td>Patients with pathologic stage III or IV head and neck squamous cell carcinoma involving the oral cavity, oropharynx (p16 negative), larynx, or hypopharynx. Must have at least 1 of high-risk pathologic feature: extracapsular nodal extension or invasive cancer within 3 mm of the primary resection margin.</td>
<td>Phase II: To select the better experimental arm to improve disease-free survival over the control arm of radiation and cisplatin</td>
<td>675</td>
</tr>
<tr>
<td>RTOG 0920</td>
<td>Open</td>
<td>A Phase III Study of Postoperative Radiation Therapy (IMRT) +/- Cetuximab for Locally-Resected Squamous Cell Carcinoma of the Oral Cavity, Oropharynx, or Larynx; Clinical Stage</td>
<td>Resected squamous cell carcinoma of the oral cavity, oropharynx, or larynx; clinical stage</td>
<td>Test whether the addition of cetuximab to radiation therapy will improve overall survival</td>
<td>700</td>
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(continued)
<table>
<thead>
<tr>
<th>Trial Name</th>
<th>Status</th>
<th>Trial Title</th>
<th>Tumor Type</th>
<th>Primary Objective</th>
<th>Accrual Target</th>
</tr>
</thead>
<tbody>
<tr>
<td>Advanced Resected</td>
<td>Open</td>
<td>Head and Neck Cancer</td>
<td>T2-T4a, N0-2, M0 or T1, N1-2, M0.</td>
<td>in postoperative patients with intermediate risk following surgery. Determine the feasibility of conducting a cooperative group prospective clinical trial in patients with resected malignant salivary gland tumors. Acquire preliminary efficacy data comparing postoperative radiotherapy alone to concurrent chemotherapy and radiation using weekly cisplatin.</td>
<td>120</td>
</tr>
<tr>
<td>RTOG 0912</td>
<td>Open</td>
<td>A Randomized Phase II Study of Concurrent Radiation and Chemotherapy Alone</td>
<td>Salivary gland carcinoma involving the major or minor salivary glands of the head and neck. Histology includes intermediate- or high-grade adenocarcinoma or mucoepidermoid carcinoma, high-grade acinic cell carcinoma, or high-grade adenoid cystic carcinoma; patients are status post curative-intent surgical resection and are found to have the following risk factors: T3-4, N1-3 disease, or T1-2 N0 with positive or close margins</td>
<td>Evaluate the safety of radiation, paclitaxel, and pazopanib suspension. Evaluate and compare overall survival at 1 y from study registration.</td>
<td>110</td>
</tr>
<tr>
<td>NRG HN001</td>
<td>Open</td>
<td>Randomized Phase II and Phase III Studies of Individualized Treatment for Nasopharyngeal Carcinoma Based on Biomarker Epstein Barr Virus (EBV) DNA</td>
<td>Stage II-IVB nasopharyngeal cancer with detectable plasma Epstein-Barr virus DNA</td>
<td>Phase II: cisplatin/SFU vs gemcitabine/paclitaxel as adjuvant chemotherapy for nasopharyngeal cancer</td>
<td>758</td>
</tr>
<tr>
<td>ECOG 1311</td>
<td>Open</td>
<td>Phase II Trial of Afatinib as Adjuvant Therapy Following Chemoradiation in Patients with Head and Neck Squamous Cell Carcinoma at High Risk of Recurrence</td>
<td>Stage III/IV head and neck squamous cell carcinoma following chemoradiation therapy and any surgical salvage therapy</td>
<td>Determine efficacy of afatinib as adjuvant following chemoradiation therapy and surgical salvage</td>
<td>108</td>
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91% and would suggest that one or both of the treatment arms could be evaluated for inclusion in a future phase III study of treatment deintensification.

**Role of Transoral Surgery**

The last few years have seen an increase in the use of transoral surgery in the management of head and neck cancer as a result of increased application of transoral robotic surgery to management of OPSCC. Although transoral resection itself is not new, the most appropriate setting in which to employ these techniques has not been defined. Prior to transoral robotic surgery, transoral resection was performed through many methods, including traditional bovic electrocautery and transoral laser microsurgery. Transoral surgery offers a less morbid surgical approach that has the potential to allow for less toxic and equally successful treatment in good prognosis patients. It also offers the possibility of an increase in locoregional control for patients with OPSCC caused by substance abuse, who more frequently develop locoregional recurrence despite aggressive chemoradiotherapy. As the use of transoral surgery has increased in application, incorporation into a comprehensive treatment strategy of pharyngeal cancer has been ongoing. In 2011, the NCI sponsored a meeting to develop clinical trial strategies to best incorporate transoral surgery into the multidisciplinary care of the OPSCC patient. Two trials employing transoral surgery—one for HPV OPSCC and one for non-HPV OPSCC—are now open and enrolling patients. Where possible, harmonization has also taken place between both trials in such areas as defining a common standard for clear resection margins (ie, at least 3 mm) sufficient to withhold adjuvant radiotherapy. ECOG 3311 is a phase IIIR study of transoral resection, followed by risk-adapted adjuvant therapy for HPV OPSCC. Patients with cT1-2, N1-2b p16-positive OPSCC—a group that has generally been treated with definitive concurrent chemoradiotherapy—are treated with transoral resection and neck dissection. They are then allocated to “risk groups” based on surgical pathology. High-risk patients—positive margins, ≥5 positive lymph nodes, or >1 mm of extracapsular spread of lymph nodes—receive standard adjuvant chemoradiation (66 Gy) therapy with weekly cisplatin. Patients with low-risk tumors—clear margins at least 3 mm and either N0 or N1 neck disease—receive no further treatment, also considered standard. The intermediate-risk group—clear or close margins <3 mm with <1-mm extracapsular spread in lymph nodes, 2 to 4 metastatic lymph nodes, or perineural or lymphovascular invasion—will be randomized to receive either standard-dose postoperative radiation (60 Gy) or reduced-dose radiation (50 Gy). The intent of the trial is, first, to ascertain whether intermediate-risk HPV-positive tumors can be treated with less aggressive radiation while deriving acceptable survival and functional results and, second, to identify how often radiation and/or chemotherapy can be avoided in patients undergoing initial low-morbidity surgery. For the latter, it will also be first time that a common criterion for a clear resection margin will be applied to permit omission of adjuvant radiotherapy in a randomized clinical trial setting.

RTOG 1221 is a randomized phase IIIR trial of surgery versus chemoradiation for HPV-negative oropharynx cancer. Many of these cancers recur after nonsurgical management with concomitant chemoradiation, but surgical salvage of such recurrent oropharynx cancer has been disappointing. The goal of this trial is to define the efficacy and side effects of initial concomitant chemoradiation with weekly cisplatin versus primary transoral surgery and neck dissection, followed by risk-adapted adjuvant treatment. Survival and quality of life are both study end points. This is the first prospective trial that seeks to determine the treatment results of resection versus chemoradiation in identical patient populations and define the potentially different side effects of treatment. This study will help determine whether surgery can offer benefit in non–HPV OPSCC and should provide important quality-of-life data surrounding resection and nonsurgical management of OPSCC. As with ECOG 3311, the common criterion of a 3-mm resection margin will be informative to guide future guidelines for omission of adjuvant radiotherapy.

Another critical part of both these trials is defining surgical quality. Surgeons must qualify to enroll patients in these trials by submitting cases for external review. They must demonstrate a history of successful transoral resections, including adequate lymph node resection and acceptable transoral margin status with sufficiently low morbidity. In addition to surgical quality, patient quality of life and functional outcomes such as swallowing will be measured in both protocols. Direct comparison of quality-of-life and functional outcomes between surgically and nonsurgically treated OPSCC patients has been difficult largely due to patient selection bias. Both randomized trials will capture these data to provide a clearer picture of the quality-of-life and functional outcomes of the different treatment modalities.

Finally, while prior trials have used higher-dose every-3-week dosing of cisplatin, both these trials utilize weekly cisplatin therapy. The total dose administered, 40 mg/m²/wk for 6 to 7 weeks, is equivalent to or higher than the every-3-week regimens based on 100 mg/m² every 3 weeks. Despite the absence of phase III data demonstrating comparability to every-3-week dosing, this regimen is now used in large part because of its improved tolerability in the community. This movement toward studying weekly cisplatin in trials represents a shift in head and neck trials utilizing chemoradiation.

**Improving Postoperative Adjuvant Chemotherapy**

Bernier and Cooper’s combined analysis of European Organisation for Research and Treatment of Cancer and RTOG data showed that patients with positive margins or nodal extracapsular spread were those mostly likely to benefit from adjuvant chemoradiotherapy, compared to adjuvant radiation alone, after surgery. However, adjuvant-concomitant chemoradiation with cisplatin after surgery has documented higher treatment toxicity and as-yet-unexplained late
RTOG 1216 is a randomized phase II/III trial of postoperative chemoradiation for patients at high risk of recurrence. It is based on earlier phase II results from RTOG 0234 that suggested benefit from alternative docetaxel and cetuximab adjuvant chemoradiotherapy regimens. Following resection of a high-risk head and neck squamous cell carcinoma (with nodal extracapsular spread or less than 3 mm margins), patients are randomized to 1 of 3 arms. The control arm is adjuvant radiation therapy with weekly cisplatin; the second arm is adjuvant radiation with weekly docetaxel; and the third arm is adjuvant radiation with docetaxel and cetuximab. After initial accrual designed to identify the most promising regimen between the second and third arms, the phase III part of this study will determine whether it is superior to the control arm.

RTOG 0920 is a randomized trial of adjuvant postoperative radiation therapy versus radiation therapy and cetuximab for patients with intermediate risk of recurrence. Such tumors do not meet the Cooper and Bernier definition of high risk, and they are characterized by perineural invasion, angiolymphatic invasion, at least N2a or higher neck disease without extracapsular spread, close margins (<5 mm), T3/T4a primary tumors, or thick (>5 mm) T2 oral cavity cancers. Historically, these patients have been treated with postoperative radiation therapy alone. This phase III study will evaluate whether treatment escalation with the addition of cetuximab to radiation offers benefit for patients with such intermediate risk tumors.

**Rare Head and Neck Malignancies**

Optimum treatment of rare head and neck tumors remains a challenge for any treatment team. Single-institution retrospective experiences compromise the bulk of published experiences, so questions surrounding treatment of these uncommon diseases persist. In response, the North American head and neck cancer therapeutic community has mounted trials to evaluate 2 rare malignancies: salivary gland cancers and anaplastic thyroid cancer.

Following complete surgical resection, patients with high-risk salivary gland cancers often receive adjuvant radiation to improve locoregional control. The role of adjuvant chemoradiation has been studied little, and only limited data are available surrounding efficacy. RTOG 1008 is a randomized trial comparing adjuvant postoperative radiation to postoperative chemoradiation with concurrent cisplatin for high-risk malignant salivary gland cancers. This trial has rapidly accrued and will soon be closed to patient entry, with results available in the next several years.

RTOG 0912 is a randomized phase II trial of radiation therapy with concurrent paclitaxel alone or with the addition of pazopanib in the treatment of anaplastic thyroid cancer. Anaplastic thyroid cancer has a dismal prognosis, and treatment options for the disease are limited. Pazopanib is a multitargeted tyrosine kinase inhibitor with activity against c-kit, PDGF receptor, VEGF receptor, and FGF receptor. Preclinical data suggest that pazopanib, in combination with paclitaxel, may have activity in treating anaplastic thyroid cancer.

**The Importance of Biomarker-Driven, Innovative, and Targeted Investigation**

In the last decade, our knowledge of tumor biomarkers and cancer pathways, such as the EGFR signaling pathway, has grown. There has been an interest in applying this knowledge to direct clinical decision making or to develop innovative approaches. In this final section, we highlight 2 clinical trials that utilize this molecular information to either inform treatment decision making or target specific cancer pathways for treatment.

The Intergroup 0099 trial demonstrated that concomitant chemoradiation, followed by adjuvant chemotherapy, for advanced nasopharynx cancer significantly improved survival when compared to radiotherapy alone. While some nasopharynx cancers are due to alcohol and tobacco use, most are due to Epstein-Barr virus (EBV) infection. Prior data have shown that EBV DNA detectable in the plasma has prognostic implications. Patients with no detectable plasma EBV DNA after treatment have significantly better 2-year overall survival (97% vs 56%).

NRG-HN001 is a randomized phase II/III study of individualizing treatment of advanced nasopharynx cancer by plasma EBV DNA status. Patients with stage II-IVb nasopharynx cancer with detectable EBV DNA initially undergo standard concomitant chemomeration; thereafter, plasma EBV DNA is measured. Those with undetectable plasma EBV DNA are either randomized to observation only or another 3 cycles of cisplatin/5FU, the traditional conventional approach defined by the result of Intergroup 0099. This randomization arm is a phase III study to determine if the adjuvant chemotherapy with cisplatin/5FU offers benefit in these patients. A recent trial has suggested that this adjuvant chemotherapy may not offer benefit.

If patients have detectable plasma EBV DNA following chemoradiation, however, they are in the high-risk group. These patients are randomized to either standard adjuvant chemotherapy with cisplatin/5FU or an alternative regimen using gemcitabine/paclitaxel. The goal of this phase IIR arm is to determine if adjuvant chemotherapy with an alternative regimen (gemcitabine/paclitaxel) is more effective in this high-risk group.

Research has also demonstrated the role of EGFR signaling in head and neck cancer pathogenesis. Until now, small molecule tyrosine kinase inhibitors have not been a part of routine head and neck cancer treatment. Afatinib is a small molecule tyrosine kinase inhibitor that targets Her2 and EGFR kinases. ECOG 1311 is a phase IIR trial of afatinib as adjuvant therapy in patients with head and neck squamous cell carcinoma who are at high risk of recurrence. Patients are eligible for the trial if they have completed chemoradiation therapy for head and neck cancer and subsequently undergo salvage neck dissection for regional disease.
with viable tumor. They must have no evidence of primary or distant disease. Patients are randomized between either oral placebo or afatinib for 48 weeks after salvage surgery. The goal is to determine if application of this targeted agent as an adjuvant treatment will affect the rates of recurrence.

Through both these examples, one can appreciate the incorporation of molecular biomarkers and use of targeted therapy in the development of head and neck cancer clinical trials. We anticipate more such trials in the future.

Conclusions and Implications for Practice

The development of NCI-funded clinical trials has focused on several topics. The identification of HPV OPSCC as a distinct clinical entity has spawned efforts to tailor therapy for this highly curable disease. The resurgence of transoral resection for oropharynx cancers, especially HPV OPSCC, has prompted the design of trials to establish the potential benefits of modern primary surgical management of oropharynx cancers. Due to the toxicity associated with adjuvant chemoradiation using cisplatin, alternative chemotherapy regimens are being explored for intermediate- and high-risk cancers. Recognizing the importance of prospectively acquired data and the limitations of single-institution experiences, efforts are underway to study rare diseases, such as salivary gland cancers and anaplastic thyroid cancer. Finally, the application of tumor marker–driven treatment decision making, such as that seen in NRG HN001, will usher in a more personalized approach to cancer treatment.

As clinical trials continue to inform the best treatments for head and neck cancer, support by otolaryngologist and head and neck surgeons and trainees who see and diagnose these patients every day will be essential if these important clinical trials are to be completed. By reviewing the current efforts in NCI-funded clinical trial development, we hope to raise awareness of these efforts. We encourage otolaryngologists in training and practice to continue referring these patients for enrollment so that they may receive the best care and improve future patient outcomes.

Author Contributions

Jeffrey C. Liu, manuscript design, revision, final approval, and accountability; John A. Ridge, manuscript design, revision, final approval, and accountability; David M. Brizel, manuscript design, revision, final approval, and accountability; Brian O’Sullivan, manuscript design, revision, final approval, and accountability; Ezra W. Cohen, manuscript design, revision, final approval, and accountability; Bhupinder S. Mann, manuscript design, revision, final approval, and accountability; David J. Adelstein, manuscript design, revision, final approval, and accountability.

Disclosures

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References


