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| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| |  | | --- | | Table S1. Induction chemotherapy followed by chemoradiation versus chemoradiation alone in LASCCHN | | | | | | | | | | | | | | |
|  | | | **Hitt et al., Annals of Oncology 2014 [15]** | | | **Cohen et al., JCO 2014 [16]** | | **Haddad et al., Lancet Oncology 2013 [17]** | | | | | |
| **Toxicity grading scale** | | | **NCI-CTCAE**  **version 2.0** | | | **NCI-CTCAE**  **version 3.0** | | **NCI-CTCAE**  **version 3.0** | | | | | |
|  | | | **Grade 3-4 toxicities during the induction period with TPF 1** | | | | | **Grade 3-4 toxic effects during the whole treatment** | | | | | |
| **Neutropenia** | | | 19% | | | 11% | |  | | | **TPF 4 --> CRT 5** | | **CRT 6** |
| **Febrile neutropenia** | | | 17% | | | NA | | **Mucositis** | | | 47% | | 16% |
| **Asthenia/Fatigue** | | | 10.5% | | | 7.4% | | **Febrile neutropenia** | | | 23% | | 1% |
| **Decreased appetite/Anorexia** | | | 5.2% | | | 7.4% | | **Pain** | | | 3% | | 12% |
| **Vomiting** | | | 6.6% | | | 2.2% | | **Xerostomia** | | | 7% | | 7% |
| **Dysphagia** | | | 1.3% | | | 2.9% | | **Neuropathy** | | | 0% | | 3% |
| **Stomatitis/mucositis** | | | 9.1% | | | 9.00% | | **PEG tube** | | | 79% | | 85% |
| **Diarrhea** | | | 7.2% | | | 5.1% | |  | | |  | |  |
| **Infection** | | | 4.6% | | | 2.9% | |  | | |  | |  |
| **Nephropathy/Creatinine** | | | 6.5% | | | 0.7% | |  | | |  | |  |
| **Ototoxicity** | | | 0.7% | | | NA | |  | | |  | |  |
| **Neurotoxicity** | | | 0% | | | NA | |  | | |  | |  |
| **Others** | | | 26.2% | | | NA | |  | | |  | |  |
|  | | | **Toxicities grade 3-4 during CRT** | | | | |  | | |  | |  |
|  | | | **TPF --> CRT 2** | | **CRT 2** | **TPF --> CRT 3** | **CRT 3** |  | | |  | |  |
| **Neutropenia** | | | 30.2% | | 20.4% | 3.2% | 1.5% |  | | |  | |  |
| **Febrile neutropenia** | | | 4.7% | | 0,90% | NA | NA |  | | |  | |  |
| **Asthenia** | | | 6.6% | | 3.4% | 4.8% | 3% |  | | |  | |  |
| **Decreased appetite/Anorexia** | | | 1.9% | | 1.7% | 11% | 14% |  | | |  | |  |
| **Vomiting** | | | 4.7% | | 8,50% | 3.2% | 2.3% |  | | |  | |  |
| **Dysphagia** | | | 8.5% | | 4.2% | 12% | 15% |  | | |  | |  |
| **Odynophagia** | | | 13.2% | | 6.8% | NA | NA |  | | |  | |  |
| **Stomatitis/mucositis** | | | 49% | | 33% | 49% | 44.5% |  | | |  | |  |
| **Diarrhea** | | | 0% | | 0,90% | 0% | 3% |  | | |  | |  |
| **Infection** | | | 4.7% | | 4.3% | 11% | 14% |  | | |  | |  |
| **Rash/Dermatitis** | | | 4.7% | | 7.6% | 18% | 24% |  | | |  | |  |
| **Nephropathy/Creatinine** | | | 1.9% | | 5.1% | NA | NA |  | | |  | |  |
| **Ototoxicity** | | | 0.9% | | 0.9% | NA | NA |  | | |  | |  |
| **Neurotoxicity** | | | 0.9% | | 1.7% | NA | NA |  | | |  | |  |
| **Others** | | | 27% | | 31.7% | NA | NA |  | | |  | |  |
| Abbreviations: JCO: Journal of Clinical Oncology; NCI-CTC AE: National Cancer Institute-Common Toxicity Criteria for Adverse Events; PEG tube: percutaneous endoscopic gastrostomy; CRT: chemoradiation | | | | | | | | | | |  | |  |
|  | |  |
| 1. TPF: docetaxel (day 1, 75mg/m2), cisplatin (day 1, 75mg/m2 ) and 5-fluorouracil (day 1-5, 750 mg/m2/day). | | | | | | | |  | | |  | |  |
| 2. CRT: Radiotherapy, conventional fractionation, total dose of 70 Gy in 35 fractions and cisplatin 100mg/m2 on days 1, 22 and 43. | | | | | | | |  | | |  | |  |
| 3. CRT: Radiotherapy - 3D-conformal or intensity-modulated radiation therapy, total dose of 74-75 Gy, given as fractions of 0,15 Gy twice daily every other week and docetaxel, 5-fluorouracil and hydroxyurea. | | | | | | | |  | | |  | |  |
| 4. TPF: docetaxel (day 1, 75mg/m2), cisplatin (day 1, 100mg/m2 ) and 5-fluorouracil (day 1-4, 1000 mg/m2/day). | | | | | | | |  | | |  | |  |
| 5. CRT: poor responders: radiotherapy, accelerated concomitant boost over six weeks, total of 72 Gy in 1,8/1,5 Gy fractions and weekly docetaxel (20 mg/m2) for four weeks; favourable reponders: radiotherapy, coventional fractionation, total 70 Gy in 35 fractions with weekly carboplatin (AUC=1.5) for seven weeks. | | | | | | | |  | | |  | |  |
|  | | |  | |  |
| 6. CRT: radiotherapy, accelerated concomitant boost over seven weeks, total of 72 Gy in 1.8/1.5 Gy fractions and cisplatin 100 mg/m2 on days 1 and 22. | | | | | | | |  | | |  | |  |
|  | | |  | |  |
|  | | | | | | | | | | | | | |
|  | | | | | | | | | |  | |
| Table S2. Induction chemotherapy for larynx preservation | | | | | | | | | | | | | |
|  | | | **Pointreau, JNCI 2009 [31]** | | | | | | | | | | |
| **Toxicity grading scale** | | | **NCI-CTC version 2.0 during IC and RTOG scoring system for acute and late RT toxic effects** | | | | | | | | | | |
|  | | | **Acute toxicity of chemotherapy** | | | | | | | | | | |
|  | | | **TPF 1** | | | | | | **PF 2** | | | | |
| **Death due to toxicity** | | | 2.7% | | | | | | 1.9% | | | | |
| **Alopecia grade 2** | | | 19.4% | | | | | | 2% | | | | |
| **Neutropenia grade 4** | | | 31.5% | | | | | | 17.6% | | | | |
| **Febrile neutropenia** | | | 10.9% | | | | | | 5.8% | | | | |
| **Thrombocytopenia grade 3-4** | | | 1.8% | | | | | | 7.8% | | | | |
| **Creatinine elevation grade 4** | | | 0.00% | | | | | | 2% | | | | |
| **Nausea/vomiting grade 1-3** | | | 44.4% | | | | | | 44.1% | | | | |
| **Stomatitis grade 3-4** | | | 4.6% | | | | | | 7.8% | | | | |
|  | | | **Late toxicity** | | | | | | | | | | |
| **Larynx toxicity grade 4** | | | 6.2% (2 patients treated with CRT) | | | | | 13.6% (3 patients treated with CRT) | | | | | |
| **Mucous membrane grade 3-4** | | | 1.00% | | | | | 0% | | | | | |
| **Salivary glands** | | | 6.10% | | | | | 2.2% | | | | | |
| **Subcutaneous tissue** | | | 4% | | | | | 6.6% | | | | | |
| Abbreviations: JNCI: The Journal of the National Cancer Institute; NCI-CTC: National Cancer Institute-Common Toxicity Criteria; IC: induction chemotherapy; RTOG: Radiation Therapy Oncology Group; RT: radiotherapy; CRT: chemoradiation. | | | | | | | | | | | | | |
|
| 1. TPF: 3 cycles of docetaxel (75 mg/m2 day 1), cisplatin (75 mg/m2 day 1) and 5-fluorouracil (750 mg/m2 day 1-day 5), 1x/3 weeks | | | | | | | | | | | | | |
| 2. PF: 3 cycles of cisplatin (100 mg/m2 day 1) and 5-fluorouracil (1000 mg/m2 day1-day5), 1x/3weeks | | | | | | | | | | | | | |