Multidisciplinary approach for poor prognosis sinonasal tumors: Phase II study of chemotherapy, surgery, photon and heavy ion radiotherapy integration for more effective and less toxic treatment in operable/inoperable patients

Population: patients with **operable** (**SINTART-1**) or **inoperable** (**SINTART-2**) sinonasal carcinomas with poor prognosis histology

Study design: Phase II, single-arm, open-label, multicenter clinical trial designed to primarily assess the efficacy (PFS) of a multimodality treatment (induction chemotherapy, **surgery**, photon and/or heavy ion radiotherapy) of pts with **operable/inoperable** sinonasal carcinoma with **II, III, IVa** and **T4b** AJCC stage

Sample Size: **40** patients will be enrolled for **SINTART-1**

25 patients will be enrolled for **SINTART-2**

The study is conduct in collaboration with **Fondazione CNAO, Pavia** (Centro Nazionale di Adroterapia Ocologica per il trattamento dei tumori).

Histologies considered:

- Squamous Cell Carcinoma (SCC);
- Sinonasal Undifferentiated Carcinoma (SNUC);
- Small Cell Carcinoma Neuroendocrine Type (SmCCNET);
- Pure Sinonasal Neuroendocrine Carcinoma (SNEC);
- Intestinal Type Adenocarcinoma (ITAC) with a functional p53 gene;
- Esthesioneuroblastoma with differentiation grade III-IV by Hyams

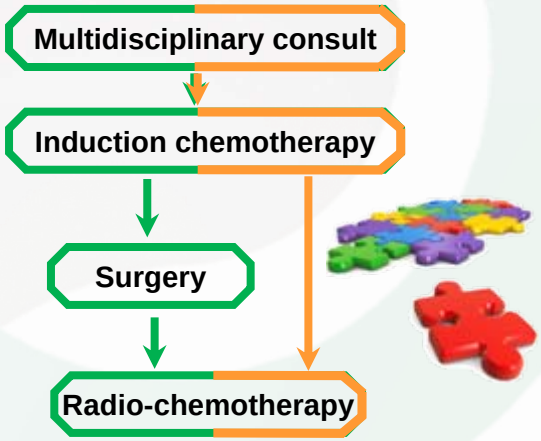
Study objectives:

Primary: - to assess the efficacy of the multimodality treatment in terms of PFS at 5 years

Secondary: - Overall Survival
- visual functionality preservation
- hearing function preservation
- to evaluate the safety of the multimodality treatment
- to assess the efficacy of the induction chemotherapy
- to evaluate late toxicities related to radiotherapy

Treatment Therapy & Follow up

Induction Chemotherapy: patients will be treated up to a max of 5 cycles and the scheme of induction CT is selected considering the histological type and molecular disease profile.
For all regimens, cycle duration is 21 days (i.e., q3w).



Surgery: surgically intervention will be planned according to initial extension of the disease **(SINTART1 only).**

Radiotherapy treatment: Photon bean therapy and/or proton/carbon ion beam therapy (i.e. heavy particle therapy) will be employed according to disease site and stage.

The choice between photons and heavy ion particles therapy will be based on comparative plans evaluation.

During IMRT radiotherapy, concurrent chemotherapy with cisplatin (100 mg/m^2 q3w or 50 mg/m^2 weekly) will be administered.

Follow Up: after the end of multimodal treatment, patients will be followed for 5 years for the evaluation of the PFS and up to a maximum of 8 years for safety