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Acronyms

IC	Intracameral
OSSN	Ocular Surface Squamous Neoplasia
IFN α -2b	Interferon alpha 2b
MMC	Mitomycin C

Definitions

- Intracameral: Inside the anterior chamber of the eye

Protocol of Interferon alpha 2b for ocular surface squamous neoplasia (OSSN)

Introduction

Ocular surface squamous neoplasia (OSSN) is the most common ocular surface malignant neoplasia and is relatively common disease worldwide. In Oman, Al-Nahdha Hospital is the main governmental centre for treating OSSN. Every year there are around 5-10 cases of OSSN seen at Al-Nahdha Hospital.

Management of this disease requires a multidisciplinary approach including ophthalmologists (anterior segment and oculoplasty), oncologists, radiologists and histopathologists. Depending on the extent of the lesion, treatment includes topical chemotherapy, systemic chemotherapy and surgery. If diagnosed early, most patients will require only topical chemotherapy.

The current available chemotherapeutic agent for treating OSSN at Al-Nahdha Hospital is Mitomycin-C (MMC). Historically this used to be the drug of choice. However, it is not the most preferred choice worldwide anymore for the following reasons:

- Severe toxicity to the ocular surface including stem cells
- Painful
- Allergy, hyperaemia
- Punctal stenosis
- Eyelid malposition
- Chemotoxic (requires special handling using gloves and wiping it out of the skin as well as discarding it on a special chemotherapy waste pin). At Al-Nahdha Hospital, this warranted admission for some patients to the hospital. Patients on average require 4 cycles of treatment before any surgery (1 week treatment, 3 weeks no treatment). This means each patient requires a total of 28 days' worth of admission.

Worldwide, IFN α -**2b** gained a lot of popularity for its better side-effects profile, tolerability and being administered on an outpatient basis; without loss of efficacy. Patient normally require daily qid dose for 3-6 months.

IFN α -2b is an immunomodulator and cellular proliferation suppressor and has been used for treatment of COVID-19, leukemia, lymphoma, malignant melanoma and chronic hepatitis B & C. The drug was available in the Ministry of Health.

The use of IFN α -2b instead of MMC for the treatment of OSSN at Al-Nahdha Hospital has several advantages⁵:

- 1) Better side-effect profile and tolerability by patients.
- 2) Better preservation of the corneal stem cells which are required for healing post-surgical removal of the lesions.
- 3) Equal or even better efficacy than MMC.
- 4) Less toxic upon handling.
- 5) Can be administered on an outpatient basis.

Aim and Objective

To develop protocol on the use of IFN α -2b for the treatment of OSSN at Al Nahdha Hospital.

Method and procedures:

Diagnosis of OSSN: OSSN can be diagnosed clinically by having a gelatinous, papillariform or leukoplaquic picture involving the conjunctiva, limbus or cornea; OR better confirmed on a histological basis though a conjunctival biopsy. UBM is recommended for clinically invasive tumours.

When to consider IFN α -2b

- IFN α -2b can be considered in patients with confirmed OSSN on conjunctival biopsy.
- IFN α -2b can be considered on clinical basis for obvious clinical OSSN especially for patients who are not fit for surgical biopsy.
- IFN α -2b is intended to be first line to replace MMC. However, MMC can be considered as second-line treatment if poor response.

- IFN α -2b can be considered as:
 - Primary treatment: IFN α -2b can be used in small tumor to fully cure them without surgical biopsy. However, surgical biopsy is recommended whenever possible to confirm the disease.
 - Neoadjuvant: This is used to chemo-reduce (shrink) the tumor prior to excisional biopsy especially if involving 6 or more clock hours of the limbus. This will ensure preservation of the stem cells in the limbus. Nevertheless, an incisional biopsy is recommended to confirm the disease prior to using IFN α -2b.
 - Adjuvant: IFN α -2b can be considered post-surgical excision especially if invasive disease or involving the surgical margin.

Who can prescribe IFN α -2b:

IFN α -2b can be prescribed by any cornea specialist after discussion with a cornea consultant.

- **Dosage:**
 - IFN α -2b is given as eye drop 1 million international per ml (1MU/MI), qid for 3-6 months or until response.
 - IFN α -2b can be considered as in subconjunctival injection (3–6 million IU/ml). However, it is associated with more systemic reactions e.g. fevers.
- **Monitoring response:**
 - The response to IFN α -2b can be monitored clinically to note the regression of the tumor by taking serial photos and documenting the size, shape or the lesion every 3-6 months
 - If inadequate response, the diagnosis should be reconsidered or trial of MMC.
 - Adverse reaction:

IFN α -2b is likely to cause mild conjunctivitis. Preservative free eyedrops can be considered alongside with it. In case of severe allergic reaction, IFN α -2b must be stopped. Please see the **figure 1**.

IFN α -2b can be prepared from a vial Lamellar airflow hood is needed as well as a dropper bottle. Preparation is the responsibility of the pharmacy.

Preparation protocol is attached in the appendix.

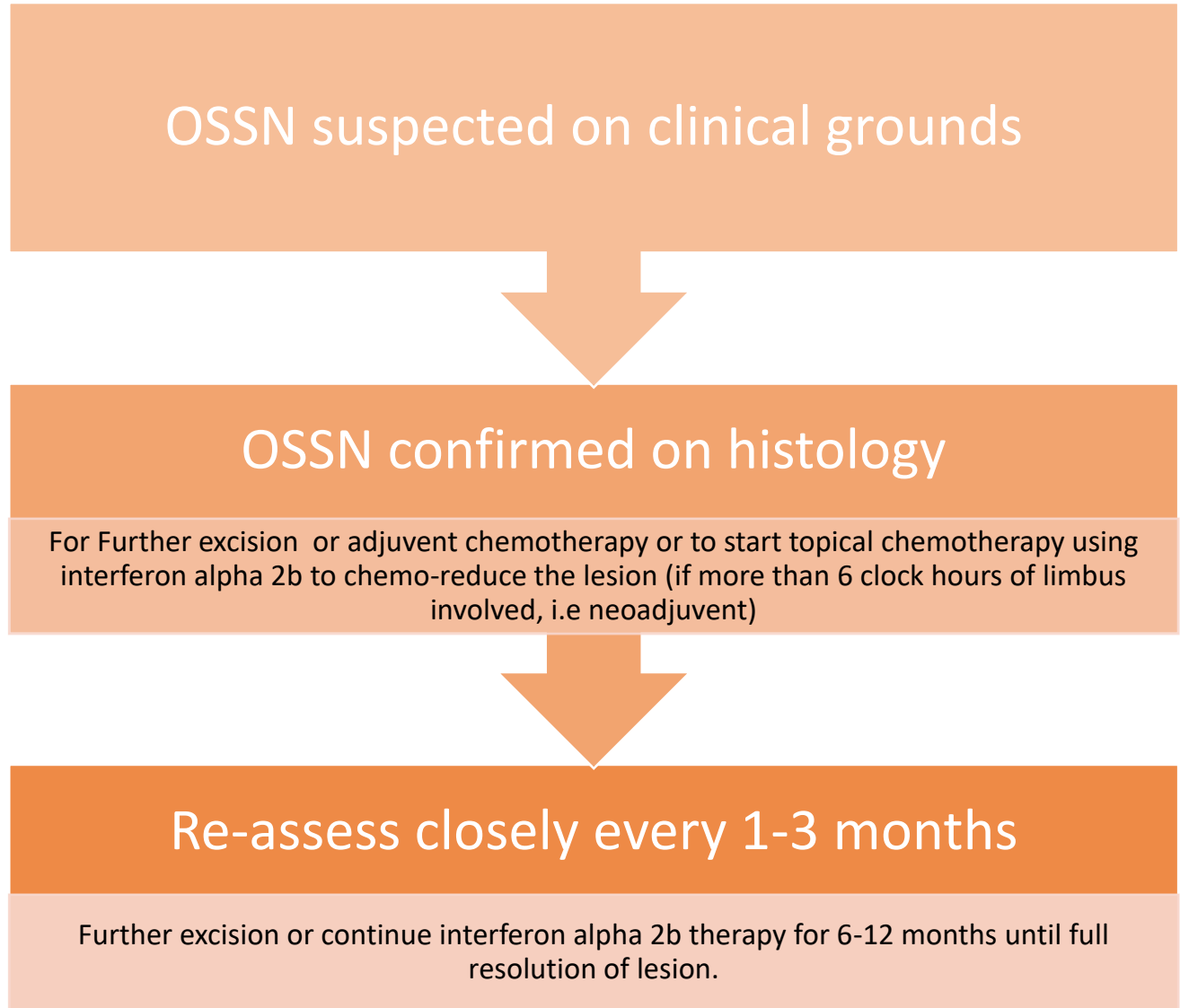
Document History and Version Control

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Figure 1



Appendix 1

9.17 Interferon Alfa-2b Ophthalmic Solution [68–80]

- **Description:**

Interferon alfa-2b is a natural glycoprotein. It has antimicrobial, antiviral and antineoplastic properties. Its role as an antineoplastic agent is due to its anti-

inducer properties of the host anti-tumor immunosurveillance. The first evidence of the efficacy of the product in treating limbal epithelial dysplasia was in 1994. Thereafter, it has become the main treatment agent of corneal and conjunctival tumors. It is used topically as ophthalmic drops and locally as subconjunctival injection. Generally, it is more tolerable than chemotherapy. However, the subconjunctival injection administration is associated with transient flu-like symptoms, while the administration of the ophthalmic drops may cause irritation, conjunctival hyperemia, reactive lymphoid hyperplasia, and follicular conjunctivitis. These side effects usually resolve after discontinuation of treatment. Additional limitation for interferon alfa-2b treatment when compared to surgery is the cost burden.

- **Use:**

- **Off-Label** topical application to treat ocular surface squamous neoplasia with less ocular toxicity than chemotherapeutic agents.
- **Off-Label** topical application to treat Acute Hemorrhagic Conjunctivitis (AHC), which is a rapidly progressive contagious viral infection.

- **Dose:**

One drop four times daily. The total length of treatment varies amongst different studies, ranging from 1 to 4 months.

- **Preparation:**

- **Interferon Alfa-2b One Million International Unit 1 MU/ml in 10 ml**

Ingredients	Quantity
Interferon Alfa-2b 10 MU/ml vial	1 ml
Distilled water used for injection (preservative-free)	9 ml

Procedure:

- Under Laminar airflow hood, transfer 1 ml from a 10 MU (10 MU/ml) vial of INTRON-A® Ready-To-Use solution to a sterile 15 ml eye dropper bottle.
- Add 9 ml of distilled water used for injection (preservative-free) to constitute a concentration of 1 MU/ml.
- The final product is stable for 14 days refrigerated.
- Cap the dropper bottle, shake to mix and label.

Expiration Date: 14 days.

Storage Conditions: Refrigerator.

Special Instructions: Keep out of reach of children. For ophthalmic use only. Keep in the refrigerator.