DEPARTMENT OF OTOLARYNGOLOGY HEAD NECK SURGERY
UNIVERSITY OF PAVIA
IRCCS POLICLINICO SAN MATTEO FOUNDATION – PAVIA
Chairman: Prof. Benazzo

Recidive dei tumori del distretto testa-collo

QUALI INDICAZIONI PER L'ECT

M. Garotta, G. Bertino,
A. Occhini, M. Benazzo

HN advanced cancer

Locoregional recurrences → clinical problem

Surgical resection, with or without adjuvant radiotherapy, provides the highest likelihood for successful salvage but…

Many patients present with unresectable disease

Systemic therapy alone provides at most a 40% response rate

These responses are commonly transient (median survival 6–9 months)

IMRT reirradiation of head and neck cancer—disease control and morbidity outcomes *E. Sulman at all, J RAd Oncol 73, 2009*

HN advanced cancer: palliation

Head and neck mucosal squamous cell carcinoma: results of palliative management

C Timon, MB, MD, FRCS ORL, K Reilly, MB

- **20 per cent of patients presenting with head and neck cancer are appropriate for palliative care**
- **Hypopharyngeal and oropharyngeal cancers form a disproportional percentage of these patients' tumours**
- **These patients survived less than six months after diagnosis**
- **Over one-third of these patients required palliative surgical treatment**

J Laryngol Otol 2006;120:389-92

HN advanced cancer: palliation

Primary end-points

Improve QoL

Produce no significant morbidities

Ability to communicate
Breathe unrestricted
Swallow
Remain pain-free
No bleed

Tracheotomy
PEG
Palliative CT/RT
PDT

ELECTROCHEMOTHERAPY

Timon C, et al. J Laryngol Otol 2006;120:389-92

ECT

History

Author	Tumor site	Patients	Objective - Complete response
Quaglino 2008	Melanoma metastases	14 pz	OR: 93% CR: 50%
Gargiulo 2009	Various H&N MTX	15 pz	OR: 100% CR: 80%
Campana 2009	Melanoma - breast cancer	52 pz 608 nodules	OR: 96% CR: 80%
Kis 2010	Melanoma MTX	7 pz 81 nodules	OR: 68% CR: 25%
Matthiessen 2011	Various	52 pz	OR: <3cm 86%; >3cm 30% CR: <3cm 68%; >3cm 23%
Curatolo 2012	Kaposi sarcoma	23 pz	OR: 100% CR: 61%

ECT: our experience

History

2009- 2010

Feasibility

Efficacy

Training improvement

2011…

EURECA Protocol

Scelsi et al. Electrochemotherapy as a new therapeutic strategy in advanced Merkel cell carcinoma of head and neck region. Radiol Oncol. 2013;47:366-369

EURECA protocol

(EUropean Research on Electrochemotherapy in head & neck CAncer)

EURECA protocol

Referral centers

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EURECA protocol

Rationale

validate the use of ECT as an alternative to standard treatments for head and neck cancer

Sample size estimation 120 pts.

EURECA protocol

Disease

Recurrent HN cancer (any type of histology). Standard treatment options must be offered to the patients

Metastatic HN cancer. Standard treatment options must be offered to the patients

Primary HN cancer (any type of histology) not eligible for surgery or radiotherapy because of patient's clinical condition or because of expectation of too large morbidity or patient's preference

Primary HN cancer in patients who refuse any other kind of treatment

EURECA protocol

Primary aim

Evaluation of tumor response (**one target lesion**) according to RECIST criteria (version 1.1) at 2 months follow-up.

Secondary aims

Safety (toxicity) of the procedure

Analysis of overall and progression free survival

“Quality of life” (EORTC QLQ-C30, EORTC QLQ-H&N35, EQ_5D)

EURECA protocol

November 2011 - March 2015

Age: 39–96 yrs (I.Q. range 66-82 yrs)

(M: 73±12 yrs, median 75 yrs)

143 patients

63 (44.1%) primaries

67 (46.9%) recurrences

13 (9,0%) mtx

Histology:

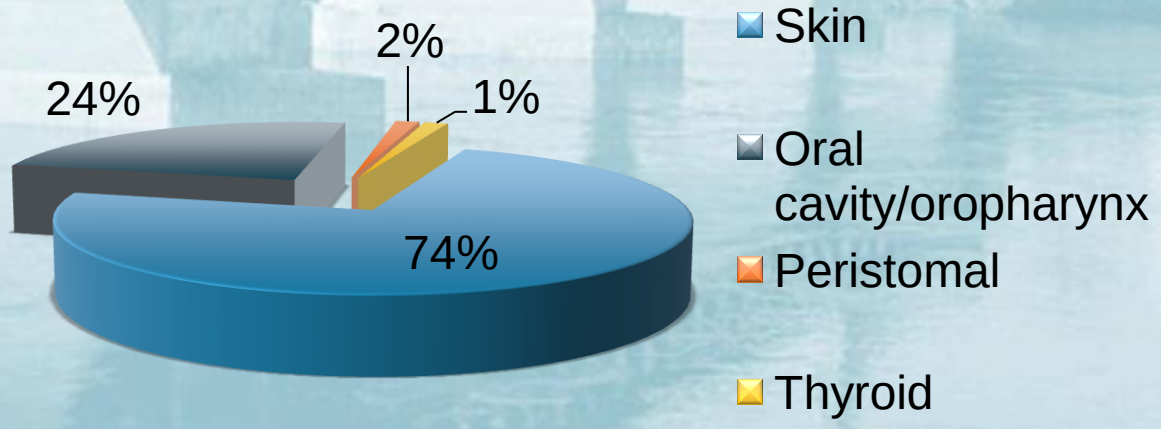
SCC 85 (59.4%)

BCC 34 (23.8%)

MM 10 (7.0%)

Other 14 (9.8%)

Localization



EURECA protocol

SITE / HISTOLOGY	< 3 cm	> 3 cm	TOTAL
Skin lesions			
BCC	31	3	34
SCC	26	24	50
MM	8	2	10
Other	4	7	11
TOTAL	**69**	**36**	**105**
Mucosal lesions			
SCC	14	19	33
Other	0	1	1
TOTAL	**14**	**20**	**34**
Peristomal lesions			
SCC	1	1	2
Thyroid lesions			
Papillary Carcinoma	0	2	2
TOTAL	**84 (59%)**	**59 (41%)**	**143 (100%)**

EURECA protocol

Analysis of response

N patients: 143 of which

- 30 in study
- 113 off study for:
  - 24 according to protocol
  - 33 progressive disease
  - 29 death
  - 11 other treatment
  - 9 unwilling/unavailable to continue (5CR, 3PR, 1SD at last follow-up)
  - 3 lost to follow-up (2CR at last follow-up, 1 without follow-up)
  - 2 adverse event
  - 2 other reasons

Patients evaluable for response: 127

EURECA protocol

Response: BCC

RESPONSE	N° OF LESIONS	PERCENTAGE	< 3 CM	> 3 CM
CR	28	85 %	28	0
PR	2	6 %	2	0
SD	1	3 %	0	1
PD	0	0 %	0	0
NA	2	6 %	1	1
TOTAL	**33**	**100 %**	**31 (94%)**	**2 (6%)**

OR:91%

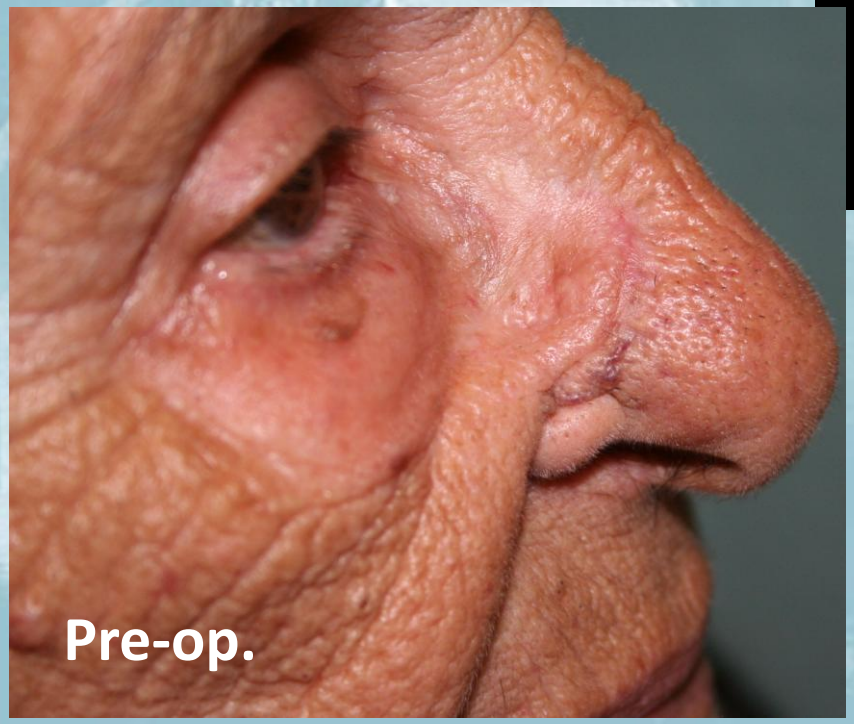
P< 0.0001

EURECA protocol

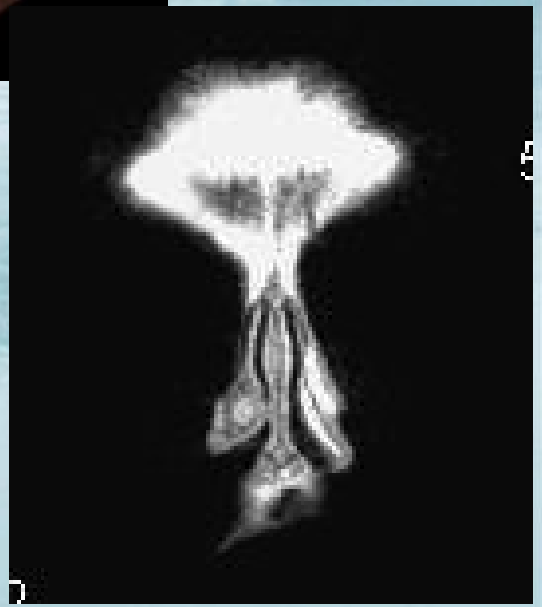
Primary BCC

EURECA protocol

Recurrent BCC



Pre-op.



EURECA protocol

Recurrent BCC

13 months after 2 cycles of ECT

EURECA protocol

Recurrent BCC

EURECA protocol

BCC: Key points

Objective response ⇑⇑

Response significantly dependent from tumor size

Possibility to consider ECT a standard treatment for BCC?

⇓

Work in progress….

EURECA protocol

Overall response (apart from BCC)

RESPONSE	N° OF LESIONS	PERCENTAGE	≤ 3 CM	> 3 CM
CR	36	37 %	26	10
PR	32	34 %	12	20
SD	17	18 %	7	10
PD	7	8 %	0	7
NA	2	3 %	1	1
TOTAL	**94**	**100 %**	**46 (49 %)**	**48 (51%)**

OR:71%

p= 0.0023

EURECA protocol

Response on skin cancer (apart from BCC)

RESPONSE	N° OF LESIONS	PERCENTAGE	≤ 3 CM	> 3 CM
CR	29	47 %	23	6
PR	17	27 %	5	12
SD	9	15 %	5	4
PD	4	6 %	0	4
NA	3	5 %	1	2
TOTAL	**62**	**100%**	**34**	**28**

OR:74%

P=0.0020

EURECA protocol

Response on mucosal lesions

RESPONSE	N° OF LESIONS	PERCENTAGE	≤ 3 CM	> 3 CM
CR	5	18 %	3	2
PR	13	46 %	7	6
SD	7	25 %	1	6
PD	3	11 %	0	3
NA	0	0 %	0	0
TOTAL	**28**	**100 %**	**11**	**17**

OR:62%

p=n.s.

EURECA protocol

Response: SCC

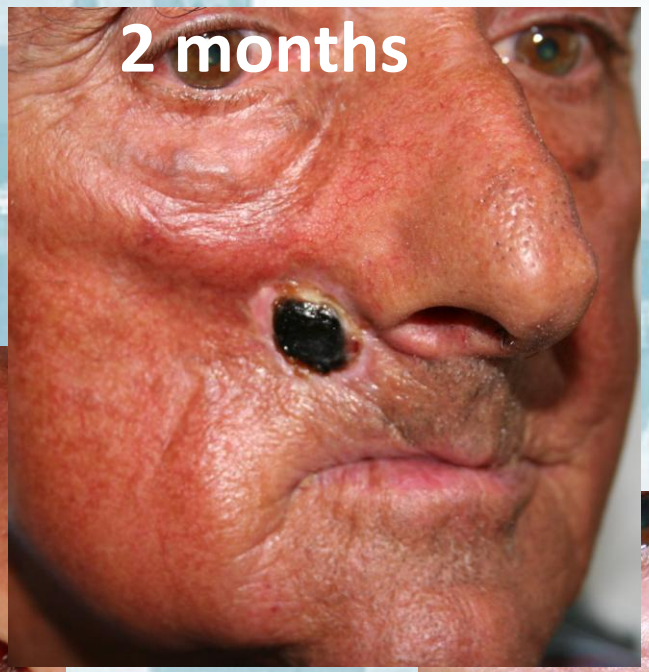
RESPONSE	N° OF LESIONS	PERCENTAGE	≤ 3 CM	> 3 CM
CR	31	42 %	22	9
PR	24	32 %	9	15
SD	12	16 %	4	8
PD	5	7 %	0	5
NA	2	3 %	1	1
TOTAL	**74**	**100 %**	**36 (49%)**	**38 (51%)**

OR:74%

p= 0.0102

EURECA protocol

Primary SCC

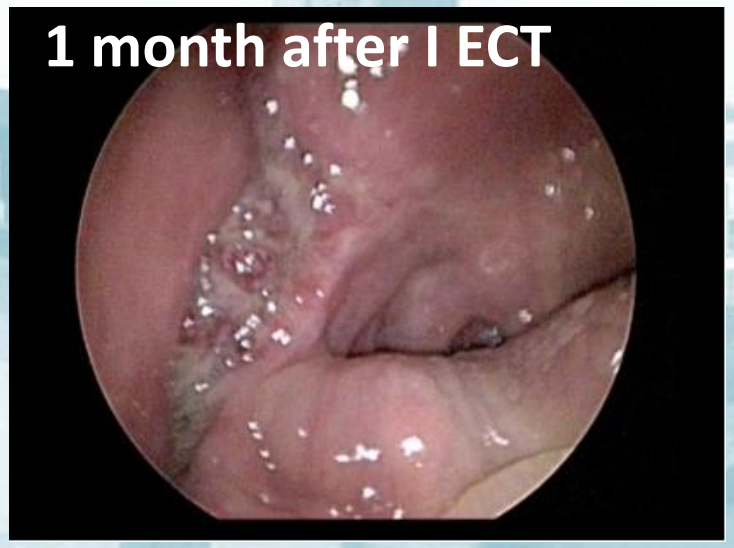


Successful cases

Primary SCC in pt with metastases from bowel adenoca.

EURECA protocol

Recurrent SCC



EURECA protocol

Response: Melanoma

RESPONSE	N° OF LESIONS	PERCENTAGE	≤ 3 CM	> 3 CM
CR	5	56 %	4	1
PR	2	22 %	2	0
SD	1	11 %	1	0
PD	1	11 %	0	1
NA	0	0 %	0	0
TOTAL	**9**	**100 %**	**7 (78%)**	**2 (22%)**

OR:78%

p= n.s.

EURECA protocol

Response: other histologies

RESPONSE	N° OF LESIONS	PERCENTAGE	≤ 3 CM	> 3 CM
CR	0	0%	0	0
PR	6	55 %	1	5
SD	4	36 %	2	2
PD	1	9 %	0	1
NA	0	0 %	0	0
TOTAL	**11**	**100 %**	**3 (27%)**	**8 (73%)**

OR:55%

p= n.s.

EURECA protocol

Metastatic carcinoma of the rhinopharynx

EURECA protocol

Metastatic carcinoma of the rhinopharynx

EURECA protocol

All other histologies: Key points

Objective response  (SCC > Others)

Response apparently not dependent from tumor size (except for SCC and skin cancer)

Mucosal lesions: difficulty in reaching the deep margins

Difficulties in treatment

Oral cavity and Oropharynx:

- Actual electrodes don’t allow an optimal access to the neoplasm to be treated
- Soft tissues of these regions mask the feed back about penetration of needles

work in progress with IGEA in developing new shapes of electrodes

Difficulties in treatment

Treatment of the scalp: tissues thinness above the bone

prevents optimal electroporation

IGEA is developing new kind of flat electrode

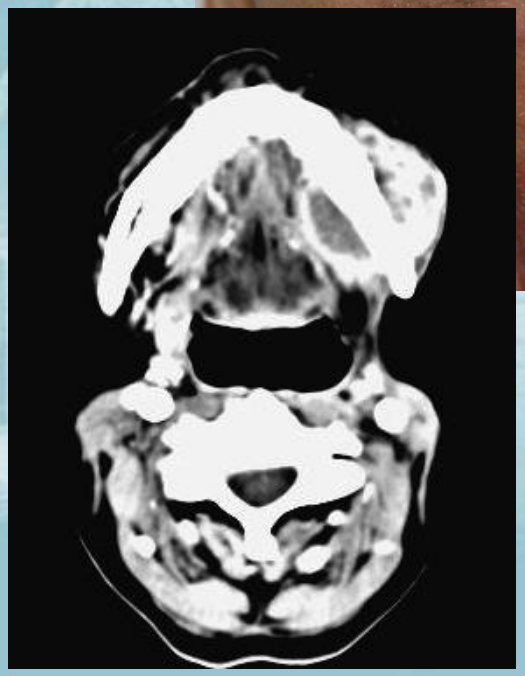
Difficulties in treatment

Treatment of the scalp: previous bone exposure remains!

Difficulties in treatment

Advanced cheek/chin lesions

increased risk of orocutaneous fistula



Recurrent SCC

Difficulties in treatment

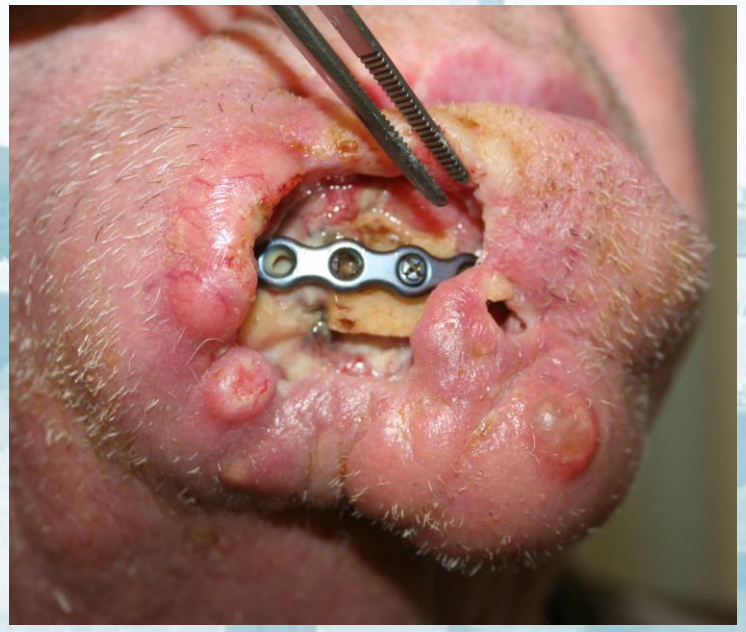
Advanced cheek/chin lesions

increased risk of orocutaneous fistula

Recurrent SCC

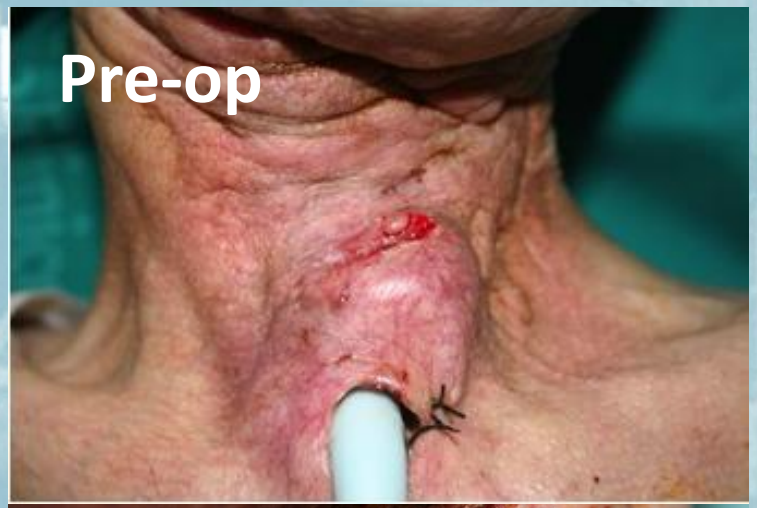
Difficulties in treatment

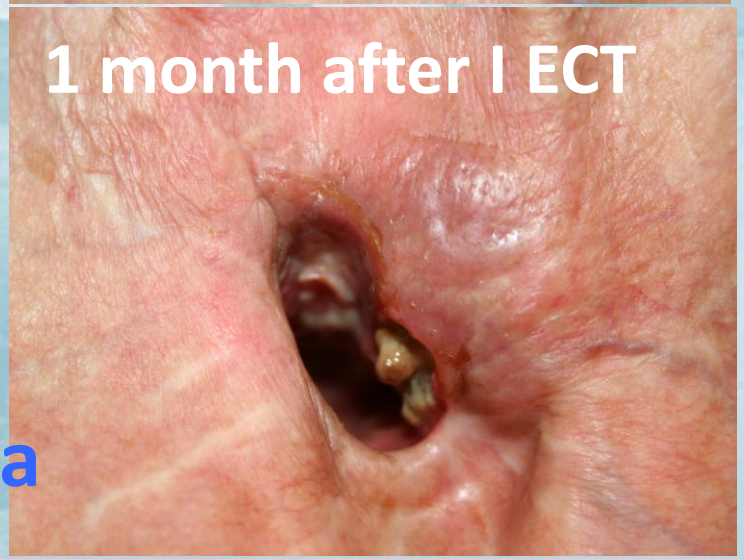
Recurrent SCC



Difficulties in treatment

Attention in treating peristomal recurrence





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EURECA protocol

CR: Survival

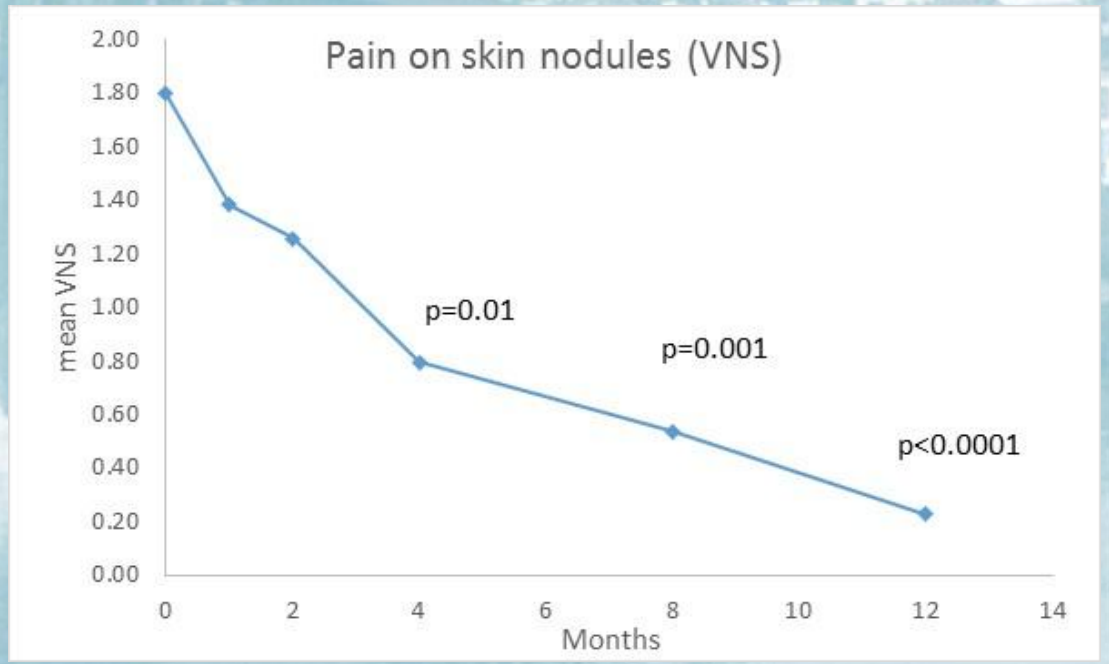
HISTOLOGY	N° OF PATIENTS	I ECT	II ECT	RECURRENCE	STATUS
BCC	28	24	3	4	25 NED, 3 AWD
SCC	30	22	8	6	18 NED, 7 AWD, 3 DWD, 2 DOD
MM	5	5	0	0	2 NED, 2 AWD, 1 DWD
OTHER	0	0	0	0	0
TOTAL	**63 (100 %)**	**51 (81 %)**	**11 (17 %)**	**10 (16 %)**	**45 NED (72%), 12 AWD (19%), 4 DWD (6%), 2 DOD (3%)**

NED= no evidence of disease; AWD= alive with disease; DWD= died without disease; DOD= died of disease; DSD= died with stable disease (died for other reasons); DUN= died for unknown reason

EURECA protocol

Pain analysis

PAIN VAS	SKIN NODULES	
	M ± SD	p value
PRE-ECT	1.8 ± 2.5	
1 MONTH F-U	1.4 ± 2.4	0.1257
2 MONTHS F-U	1.3 ± 2.3	0.0819
4 MONTHS F-U	0.8 ± 2.2	0.0097
8 MONTHS F-U	0.5 ± 1.5	0.0008
12 MONTHS F-U	0.2 ± 0.9	0.0000

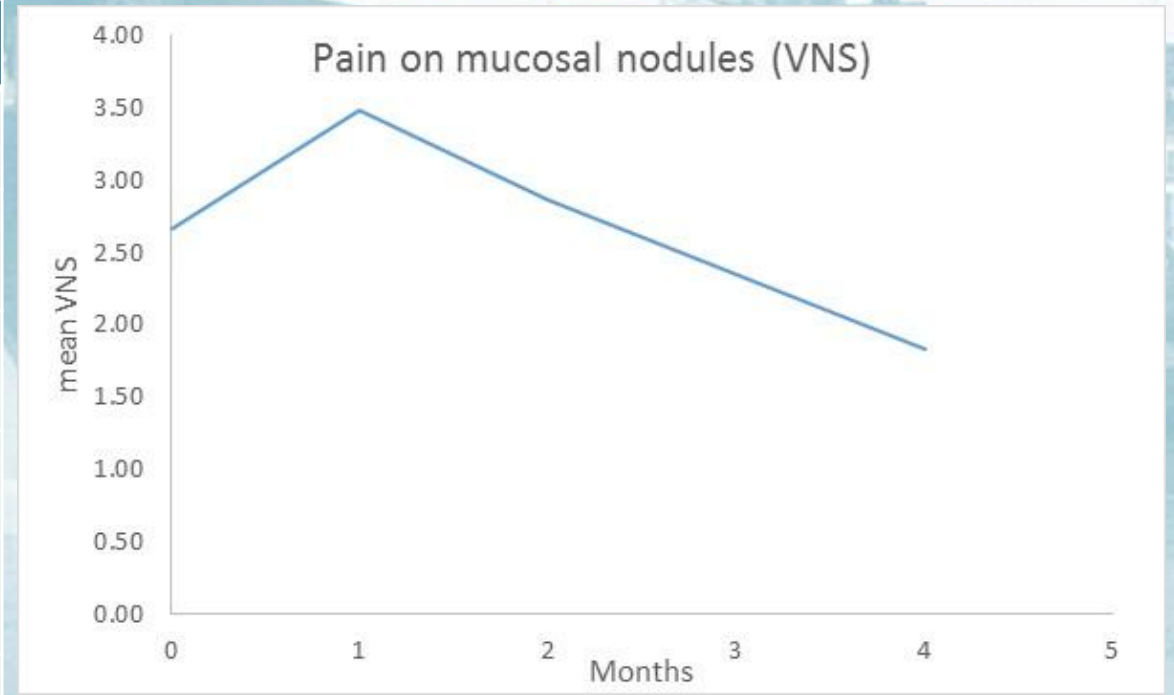


Quaglino et al. Predicting patients at risk for pain associated with electrochemotherapy. Acta Oncol. 2015;54:298-306

EURECA protocol

Pain analysis

PAIN VAS	MUCOSAL NODULES	
	M ± SD	p value
PRE-ECT	2.7 ± 2.6	
1 MONTH F-U	3.5 ± 3.1	0.1598
2 MONTHS F-U	2.9 ± 3.1	0.4223
4 MONTHS F-U	1.8 ± 2.4	0.2333
8 MONTHS F-U		
12 MONTHS F-U		



Quaglino et al. Predicting patients at risk for pain associated with electrochemotherapy. Acta Oncol. 2015;54:298-306

ECT

ADVANTAGES

- ✓ Simple and short (1H)
- ✓ Effective after one session for small lesions (< 1 / 1,5 cm)
- ✓ Treatment of not surgical lesions or resistant to chemoradiation
- ✓ Organ sparing
- ✓ Low doses of drug
- ✓ Mild side effects
- ✓ Repeatable and day surgery treatment
- ✓ Good cost/benefit ratio

DISADVANTAGES

- ✓ Only local control of disease
- ✓ Muscle contraction
- ✓ Pain during pulses delivery

EURECA protocol: preliminary conclusions

Palliation

Well established

Control of tumor growth

Control of pain

Vascular lock

EURECA protocol: preliminary conclusions

Palliation → **Well established**

Curative → **Promising results**

Organ and function sparing

EURECA protocol: preliminary conclusions

Palliation → **Well established**

Curative → **Promising results**

Neo-Adiuvant
Adiuvant → **Work in progress**

Save the date

1st World Congress on Electroporation

and Pulsed Electric Fields in Biology, Medicine and Food & Environmental Technologies

Portorož, Slovenia

6 to 10 September 2015

Grand Hotel Bernardin

Portorož