



REDUCING THE BURDEN OF SCC IN FANCONI ANEMIA

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FANCONI ANEMIA













FACTS – SQUAMOUS CELL CARCINOMA IN FA

- Squamous cell carcinoma is known to be a life-threatening complication in patients with FA.
- Compared to the average population, even without the main risk factors the risk is highly increased in FA.



Alter et al., Hematologica 2018; 103(1): 30-39





FACTS – SQUAMOUS CELL CARCINOMA IN FA

• FA patients after a BMT seem to be at higher risk and the age of onset seems to be younger.

Rosenberg et al., Blood. 2005; Jan 1;105(1):67-73 Kutler et al., Laryngoscope. 2016; 126:870-879



Alter et al., Hematologica 2018; 103(1): 30-39



FACTS – SQUAMOUS CELL CARCINOMA IN FA

- Localisations: head and neck, esophagus, vulva, cervix, anus
- There is a tendency of multiple SCCs in FA.
- Due to the underlying DNA repair defect non-surgical therapeutical options are limited.
- Poor prognosis







FACTS – SQUAMOUS CELL CARCINOMA IN FA IN GERMANY 1988-2004







FACTS – SQUAMOUS CELL CARCINOMA IN FA IN GERMANY 1988-2015















General population

AJCC staging system



Lee et al, JAMA Otolaryngol Head Neck Surg. 2017;143(4):395-402

RATIONALE: 5 YEAR SURVIVAL CORRELATES WITH STAGE AND IS POOR IN FA







Lee et al, JAMA Otolaryngol Head Neck Surg. 2017;143(4):395-402

Fanconi Anemia population



Kutler et al., Laryngoscope. 2016; 126(4):870-9



Normal







Normal

Initiated







Mild dysplasia



Initiated





















STUDY RESULTS 1 – MANY VISIBLE ORAL LESIONS









EARLY DETECTION CAN PREVENT CANCER MORTALITY





Molecular analysis

Cytopathology



Smetsers, Velleuer et al., Cancer Prev Res. 2015 Nov;8(11):1102-11.

Molecular analysis



Cytopathology



OPPORTUNISTIC SCREENING – CHARACTERISTICS AND DEFINITION



negative	histological negative diagnosis or low-grade oral epithelial dysplasia (OED) within 6 months		
	negative clinical course within 2 years		
positive	histological diagnosis of SCC or at least moderate OED within 6 months		
	clinical course consistent with cancer (<i>i.e.</i> , SCC therapy, definite imaging or palliative care)		

Clinico-pathological reference standard







HIGH SENSITIVITY AND NPV ARE DESIREABLE FOR SCREENING

- **Sensitivity**: Amount of correct diagnosed positive cases
- Specificity: Amount of correct identified healty cases
- Positive predictive value (PPV): How often was a positive diagnosis correct positive?
- **Negative predictive value (NPV)**: How often was a negative diagnosis correct negative?





CYTOLOGY SHOWS EXCELLENT SENSITIVITY AND NPV



	Cytology
Sensitivity	97.7% (94.5-100%)
Specificity	84.5% (81.7-87.3%)
PPV	45.4% (38.2-52.6%)
NPV	99.6% (99.1-100%)
AUC	0.911
95% CI (AUC)	0.885-0.937
p-value (AUC)	<0.001

- Sensitivity: Amount of correct diagnosed positive cases
- Specificity: Amount of correct identified healty cases
- Positive predictive value (PPV): How often was a positive diagnosis correct positive?
- Negative predictive value (NPV): How often was a negative diagnosis correct negative?





STUDY RESULTS 1 – MANY VISIBLE ORAL LESIONS









737 VISIBLE ORAL POTENTIALLY MALIGNANT LESIONS IN 279 FA PTS



hhu,





Kutler et al., Laryngoscope. 2016; 126(4):870-9





FIRST STEPS: REDUCING THE BURDEN OF SCC IN FA BY **EARLY DETECTION**



Kutler et al., Laryngoscope. 2016; 126(4):870-9



86 positive diagnosis in 30 FA patients **73% Stage II and less**



PATIENTS DIAGNOSED IN EARLY STAGES SHOW EXCELLENT SURVIVAL



Histology	Amount of	Mean FUP	Range [m]	Cause of death
	pts	[m]		
Moderate OED	2	44	30, 58	alive
Carcinoma in situ	7	57	7 - 126	alive
T1	6	38	6 - 78	alive
Severe OED	1	36	36	other tumor
Carcinoma in situ	1	33	33	BMF
T1	2	35	16, 55	BMF
T2	3	20	17, 20, 49	oral SCC
Т3	2	13	12, 14	oral SCC
T4	2	1	1, 1	oral SCC
palliative	4	9	7, 9, 9, 56	oral SCC



CONCLUSIONS



- Oral bush biopsy based cytology of visible lesions in 713 individuals with FA shows excellent diagnostic accuracy with high sensitivity of (97.7%).
- Due to a high negative predictive value (99.6%), invasive biopsies can be dramatically reduced by 75% (552/737) to the necessarily ones.
- Using this approach, a substantial number (73%) of squamous cell carcinoma and precursor lesions were detected at a non-invasive or early stage. Outcome in those patients diagnosed in early stages is excellent.





12 year old boy, BMT at age 6



Brush biopsy: Histology: June 2016 equivocal, broad based tretraploid stemmline negative for dysplasia





12 year old boy, BMT at age 6



Brush biopsy: Histology: June 2016 equivocal, broad based tretraploid stemmline negative for dysplasia



March 2017 not performed

negative for dysplasia



12 year old boy, BMT at age 6



Brush biopsy: Histology: June 2016 equivocal, broad based tretraploid stemmline negative for dysplasia



March 2017 not performed

negative for dysplasia



June 2018 Highly suspicious; DNA Aneuploid

1mm invasive SCC











4 weeks post OP





LET'S FIGHT CANCER









1. Information

2. Surveillance

(inspection /

documentation)

4 PROACTIVE STEPS AGAINST CANCER!

























hhu.

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supportive:

- good mouth hygiene
- self inspection every week
- regular screening by an expert
- HPV vaccination
- Healthy lifestyle (*e.g.* diet, physicial activity, mental health, resilience)





Carlberg, Front Immunol 2019



