



Where **Science** Becomes **Hope**

**SHOULD WE BE GIVING ALL  
HN SQUAMOUS CELL SKIN  
CANCERS IO PRIOR TO  
SURGERY...NO!**

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Associate Professor

DDHO July 2024



**EMORY**  
**WINSHIP**  
**CANCER**  
**INSTITUTE**

National Cancer Institute-Designated  
Comprehensive Cancer Center

**NCI**

**Designated  
Comprehensive  
Cancer Center**

**NCI**

**Comprehensive  
Cancer Center**

A Cancer Center Designated by the  
National Cancer Institute

# A MEDICAL ONCOLOGIST ARGUING AGAINST IMMUNOTHERAPY???





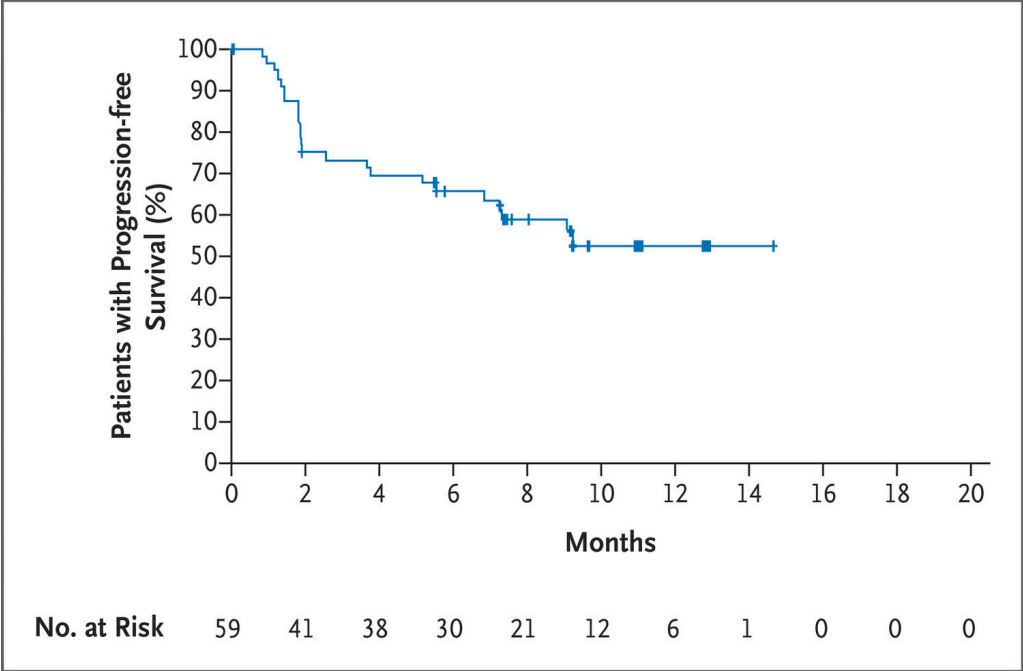
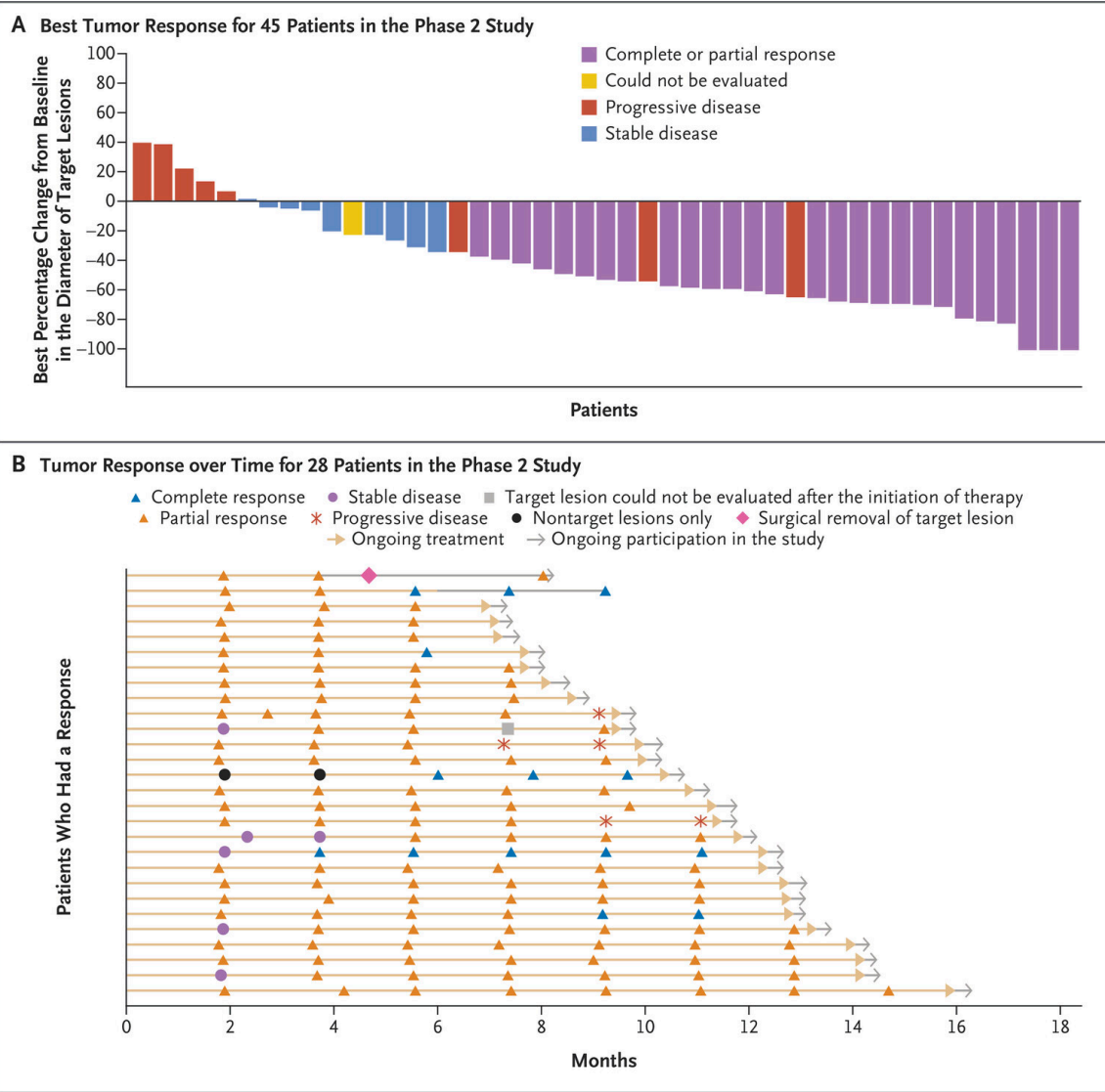
# NO EASY TASK! STRONG DEBATE COMPETITION



YOU DARE DEBATE ME?

# WHY EVEN CONSIDER IT? WORKS VERY WELL IN THE METASTATIC SETTING

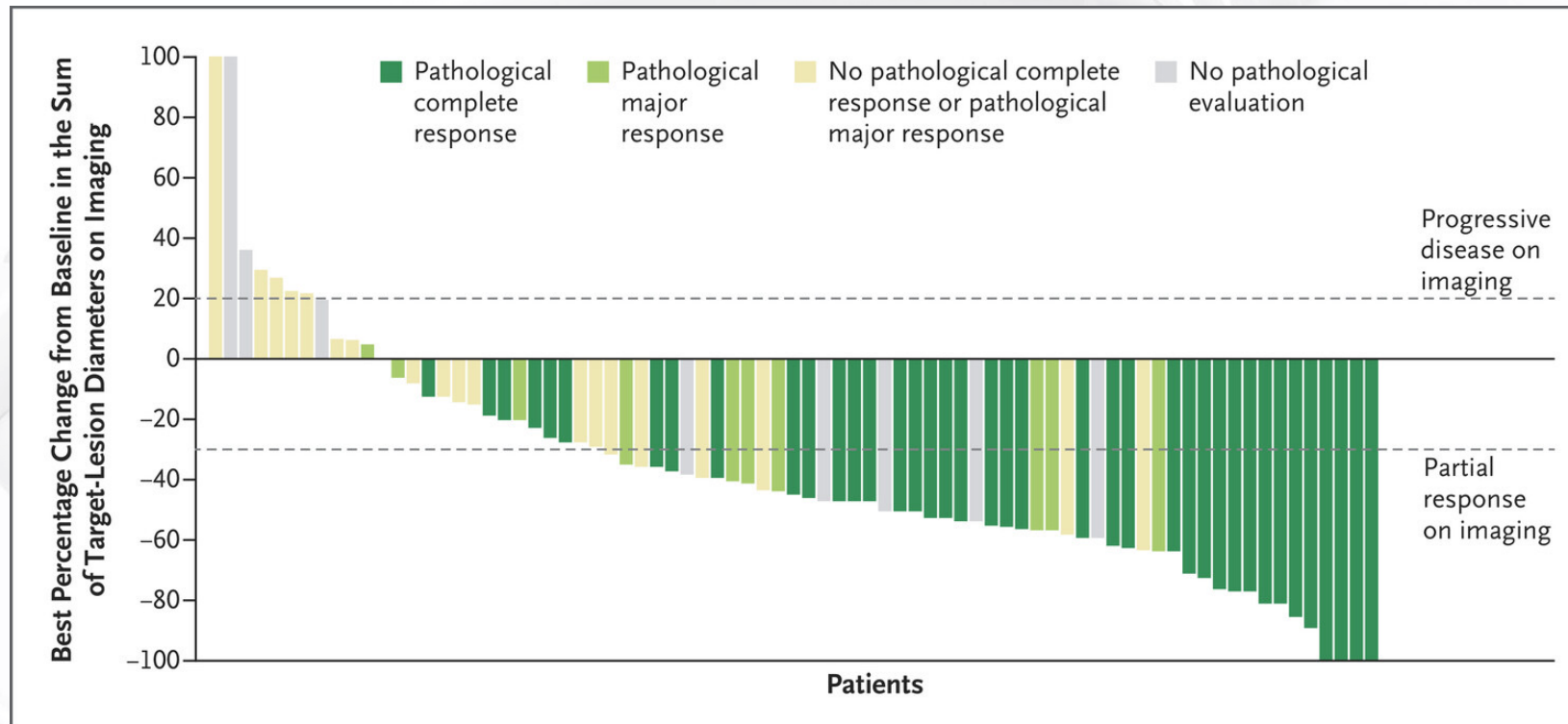
Overall Response Rate-~50%



Migen et al. NEJM 2018

# WHAT DATA IS DR EL-DEIRY GOING TO SHOW? OF COURSE GROSS ET AL.

- Single Arm Phase 2 stage 2-4 resectable cutaneous squamous cell skin cancer.
- Neoadjuvant cemiplimab given 350 mg every 3 weeks for up to four doses prior to surgery
- Primary endpoint path CR
- 79 patients enrolled, **91% HNSCC, Path CR =51%**

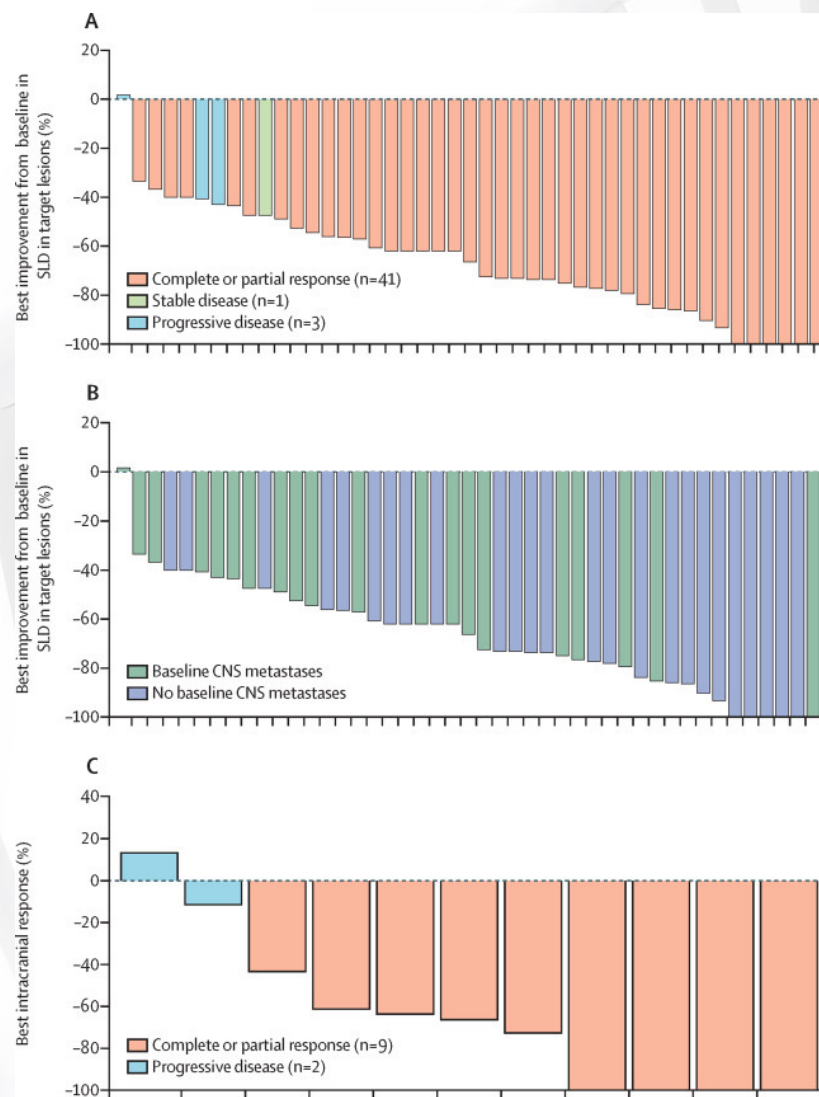


Gross et al. Lancet Onc 2023





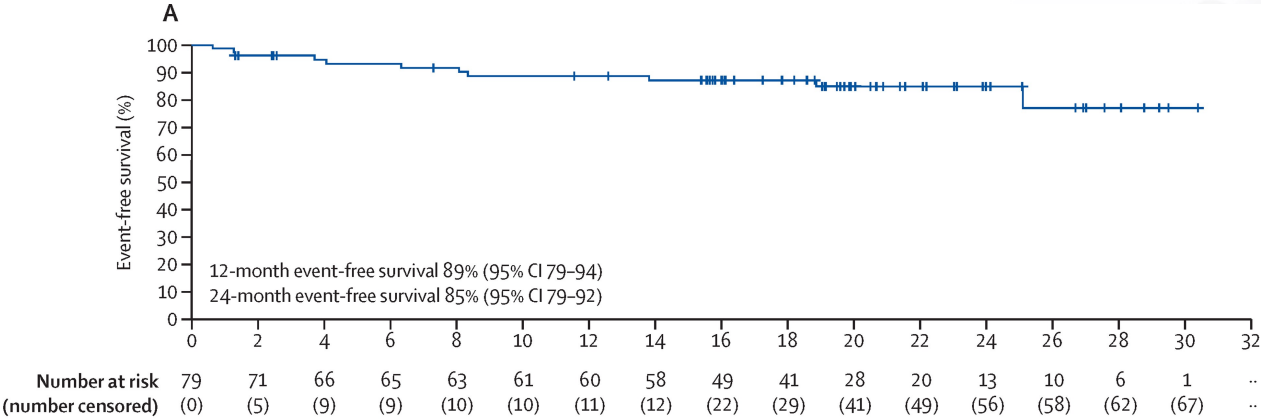
# TARGETED THERAPY IN METASTATIC DISEASE? OK FOR SINGLE ARM DATA



Entrectinib in ROS1 NSCLC

Drilon et al. Lancet 2019

# SURVIVAL DATA



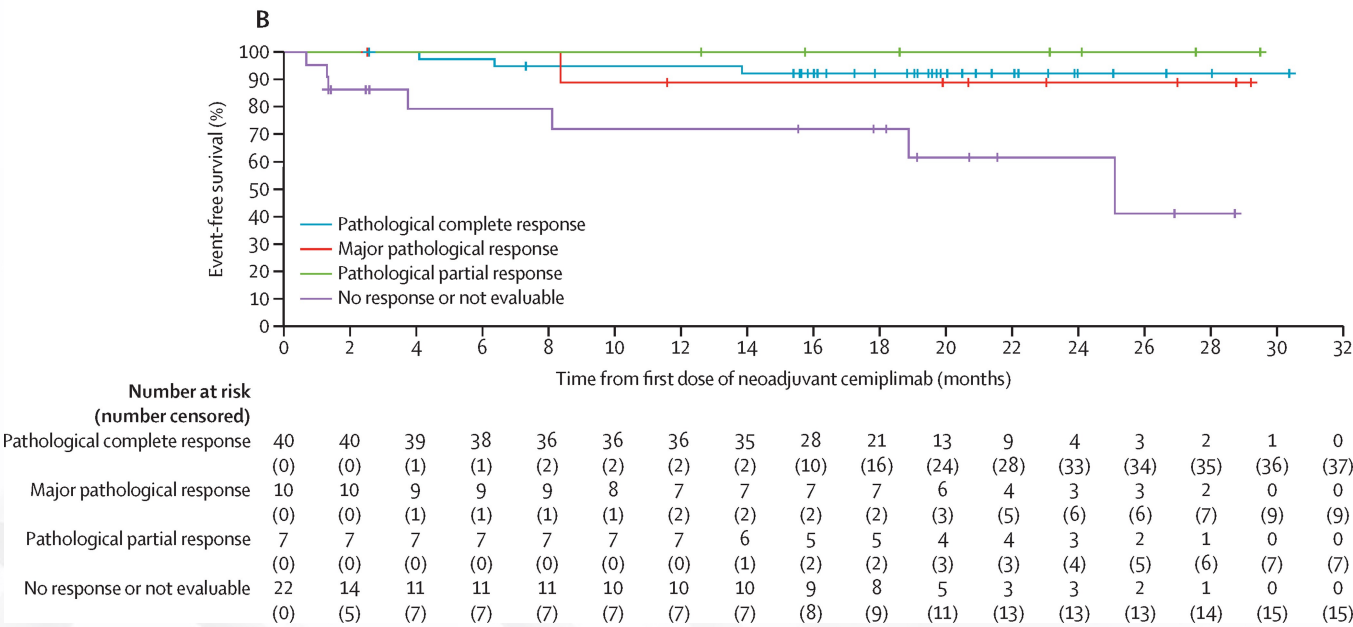
Clearly response to immunotherapy is a prognostic biomarker.

But curable disease is NOT the same as metastatic disease. Need more data!

Lack of Data that it improves survival!

Lack of Data of long term rate of local recurrence!

So what does path CR really mean?



Gross et al. Lancet Onc. 2023



# PROGRESSION/HYPERPROGRESSION IS REAL

A Patient in Phase 1 Study



Baseline



Week 6

B Patient in Phase 2 Study



Baseline

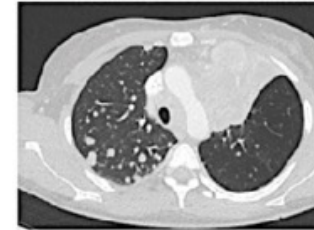


Week 8

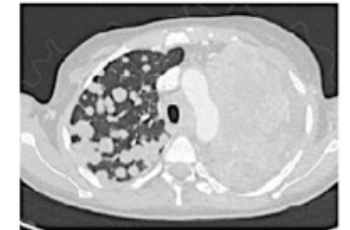
10/08/2018  
Anterior CT-scan



04/12/2018  
Baseline



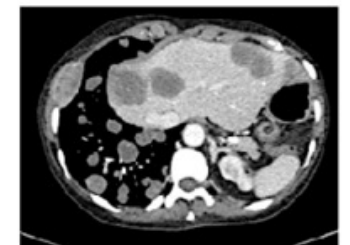
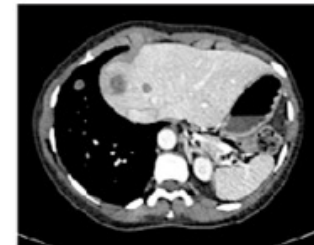
22/02/2019  
First Evaluation



Chemotherapy



Immunotherapy



-Patients had to be deemed resectable

Midgen et al. NEJM 2018  
Frelaut et al. IJMC 2019

# TOXICITY

	Grades 1–2	Grades 3			
Number of patients with any treatment-emergent adverse event	9 (56%)	4 (25%)	Superficial spreading melanoma stage unspecified	1 (6%)	0
Diarrhoea	4 (25%)	0	Dysphonia	1 (6%)	0
Fatigue	4 (25%)	0	Epistaxis	1 (6%)	0
Blood creatinine increased	4 (25%)	0	Pneumonitis	1 (6%)	0
Squamous cell carcinoma of skin*	2 (13%)	0	Productive cough	1 (6%)	0
Constipation	2 (13%)	0	Sneezing	1 (6%)	0
Pyrexia	2 (13%)	0	Dermatitis	1 (6%)	0
Alanine aminotransferase increased	2 (13%)	0	Intertrigo	1 (6%)	0
Blood alkaline phosphatase increased	2 (13%)	0	Night sweats	1 (6%)	0
Basal cell carcinoma	2 (13%)	0	Rash	1 (6%)	0
Nasal congestion	2 (13%)	0	Maculo-papular rash	1 (6%)	0
Allergic rhinitis	2 (13%)	0	Skin ulcer	1 (6%)	0
Hypothyroidism	2 (13%)	0	Hypophysitis†	0	1 (6%)
Decreased appetite	2 (13%)	0	COVID-19	1 (6%)	0
Arthralgia	2 (13%)	0	Fungal skin infection	1 (6%)	0
Pain in extremity	2 (13%)	0	Urinary tract infection	1 (6%)	0
Colitis	1 (6%)	0	Wound infection	1 (6%)	0
Dry mouth	1 (6%)	0	Hyperkalaemia	1 (6%)	0
Flatulence	1 (6%)	0	Hypocalcaemia	1 (6%)	0
Haemorrhoids	1 (6%)	0	Back pain	1 (6%)	0
Malignant melanoma*	1 (6%)	0	Anaemia	1 (6%)	0
Nausea	1 (6%)	0	Eosinophilia	1 (6%)	0
Influenza-like illness	1 (6%)	0	Cardiomyopathy‡	0	1 (6%)
Peripheral oedema	1 (6%)	0	Palpitations	1 (6%)	0
Aspartate aminotransferase increased	1 (6%)	0	Erythema of eyelid	1 (6%)	0
Blood potassium increased	0	1 (6%)	Photophobia	1 (6%)	0
Cardiac murmur	1 (6%)	0	Headache	1 (6%)	0
γ-glutamyltransferase increased	1 (6%)	0	Memory impairment	1 (6%)	0

-11% of patients did not make it to the curative therapy, surgery

-“2 had presented with bulky disease at baseline, which progressed to inoperable disease”

Will not know until a randomized trial on how these numbers impact the end patient outcomes

Gross et al. NEJM 2022

# POST OP CONFUSION

What to do after resection? How much is this affecting the survival data?

Table 1. Post-surgical management in the adjuvant phase of the study, by independent central pathology review using immune-related pathological response (n=70)

	<b>Patients with a pathological complete response* (n=40)</b>	<b>Patients with a major pathological response<sup>†</sup> (n=10)</b>	<b>Patients with a pathological partial response (n=7)</b>	<b>Patients with no response<sup>‡</sup> (n=13)</b>
Cemiplimab	12 (30%)	1 (10%)	2 (29%)	1 (8%)
Radiotherapy	1 (3%)	5 (50%)	3 (43%)	8 (62%)
Observation	24 (60%)	3 (30%)	2 (29%)	3 (23%)

Data are n (%). Investigators decided post-surgical management for individual patients based on local pathological review.

\*



## FINANCIAL TOXICITY

“The cost for cemiplimab intravenous solution (rwlc 350 mg/7 mL) is around \$10,853 for a supply of 7 milliliters”

Have to add in infusions, lab checks, toxicity management, clinic visits, extra scans post treatment.

# CONCLUSION

- EARLY data is promising, demonstrates unsurprisingly high rates of path CR
- No randomized data. While Path CR is better than no Path CR, unclear if this effects recurrence or survival(Dr El-Deiry is a great surgeon, I trust him!)
- Drugs have potential for real, life threatening toxicity
- May delay or forego the curative therapy
- Has both quality of life and financial impact
- Wild West in terms of post op treatment
- Eagerly await the randomized studies