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Title: Quality of Life in Patients With Metastatic Renal Cell Carcinoma Treated With Sunitinib or Interferon Alfa: Results From a Phase III Randomized Trial.

Background:

- The landmark study showing that Sunitinib improved response rates and progression-free survival compared to Interferon in metastatic RCC was published in the NEJM in January 2007 (356:115-24).
- Toxicity in terms of Adverse events (all grades, grade 3 and grade 4) were published and when one simply looks at the overall numbers, one could argue Sunitinib was more toxic.
- Those who have prescribed both Sunitinib and Interferon, however, realize each has its own unique toxicity profile. That paper did report on overall Health Related QOL (HR-QOL) and indicated that it was superior in the Sunitinib arm ($p < 0.001$) but the raw data was not presented.
- This current article reports the full QOL data.

Study design:

- Randomized phase III trial
 - n = 750 with 2 arms:
 - Interferon 9 mu sc tiw
 - Sunitinib 50 mg po 4 wks on / 2 wks off
 - QOL measures
 - FACT-G (assesses health related QOL for all different cancers)
 - 28 items in 4 domains (physical well being, social/family well being, emotional well being, and functional well being)
 - FACT Kidney Symptom Index (FKSI-15)
 - scored 0 (severe symptoms) to 60 (no symptoms)
 - FSKI Disease-Related Symptoms subscale (FKSI-DRS)
 - 9 questions of the total 15 questions from FKSI-15 (energy, fatigue, pain, bone pain, weight loss, shortness of breath, cough, fever, hematuria)
 - scored 0 (several symptoms) to 36 (no symptoms)
 - ie. higher scores indicate better QOL
 - EuroQOL-5D's utility score (EQ-5D Index)
 - A population preference based health state utility score
 - Based on 5 health dimensions (mobility, self-care, usual activities, pain/discomfort and anxiety/depression)
 - EuroQOL visual analog scale (EQ-VAS) for overall health state
 - Overall halth state on a visual analog scale



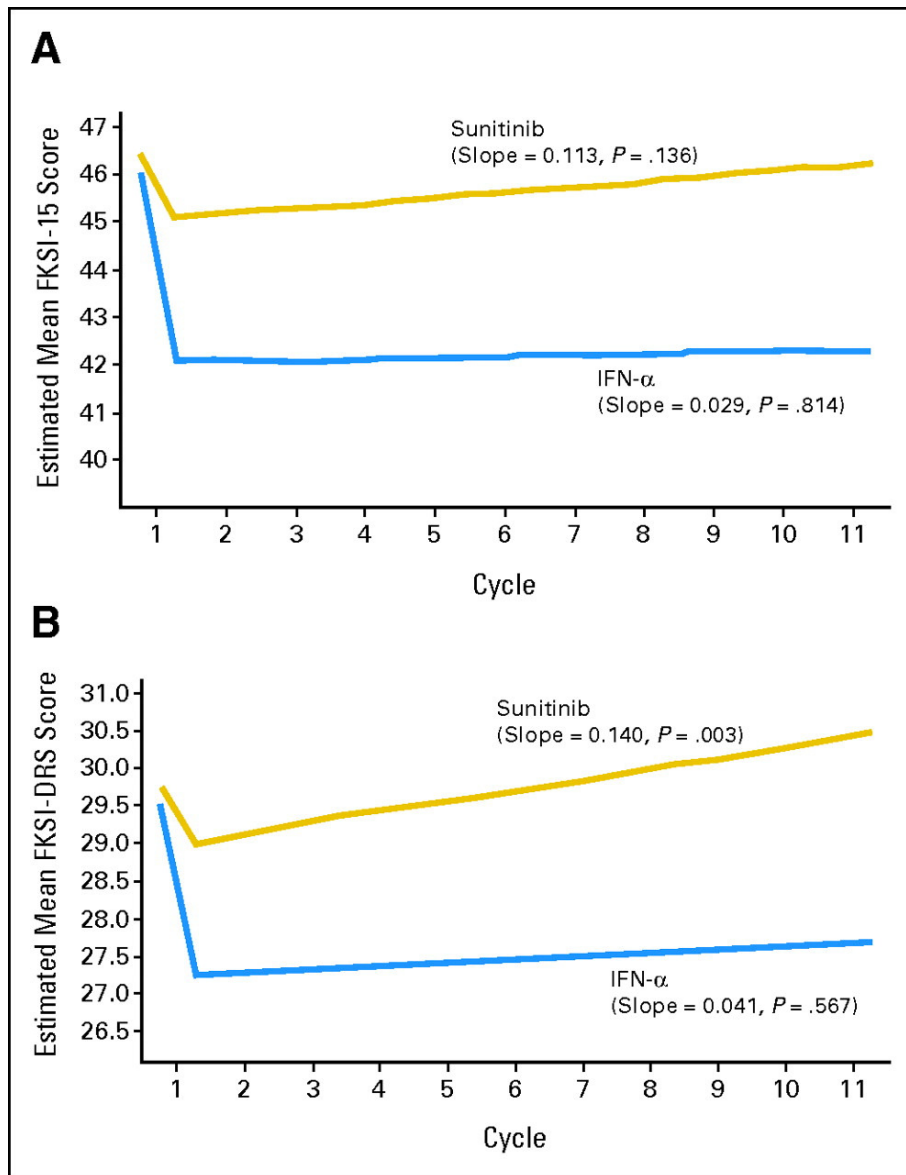
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- a 100 point VAS with 100 being the best imaginable health state
- Primary endpoint
 - FSKI Disease Related subscale

Study results:

	Sunitinib	Interferon
N	375	375
QOL Endpoints	373	356
Completion Rates for FKSI-15 and FACT-G	95.4%	95.2%

Fig 2. Estimated mean (A) Functional Assessment of Cancer Therapy–Kidney Symptom Index–15 item (FKSI-15) and (B) Functional Assessment of Cancer Therapy–Kidney Symptom Index Disease Related Symptoms (FKSI-DRS) scores by treatment arm.

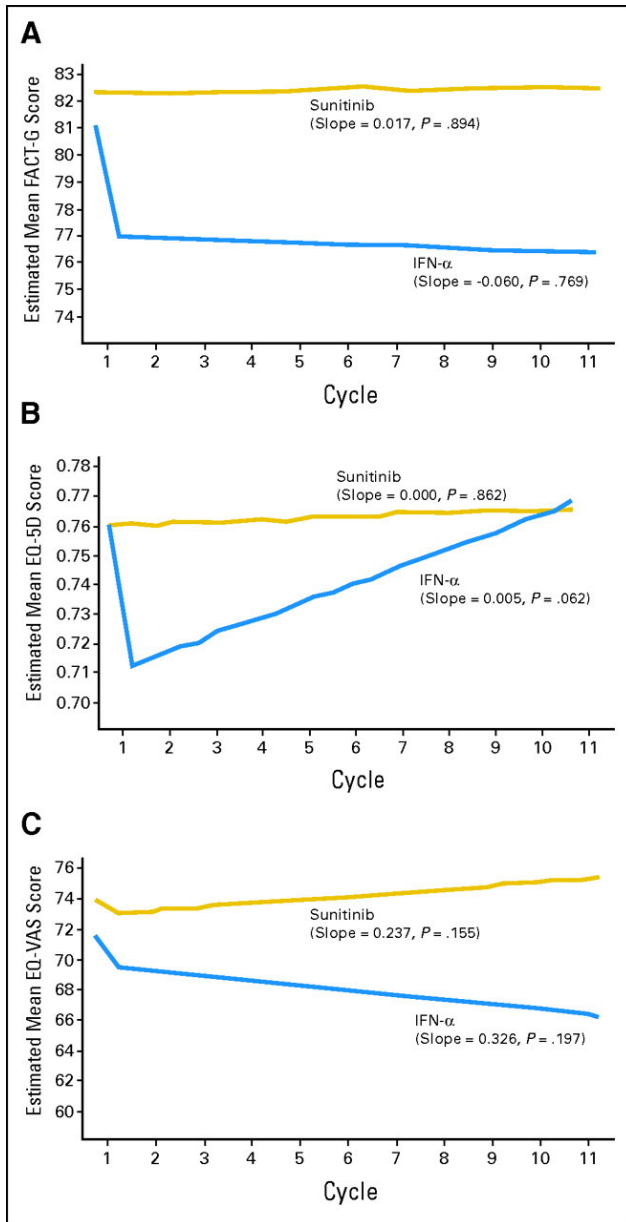


- Patients in both arms had a decrease in QOL when initially placed on Sunitinib and Interferon, but less with Sunitinib.
- Patients in the Sunitinib arm:
 - higher FKSI-15 and FKSI-DRS scores as seen in Figure 2 ($p < 0.0001$).
 - these were felt to be clinically meaningful after cycle 4, d1 for FKSI-DRS and at all time points for FKSI-15.
 - FKSI-DRS scores in the Sunitinib arm did increase over time indicating improvement in disease-related symptoms ($p = 0.003$). Specifically, the



symptoms were improvement in energy, weight, bone pain, fatigue, shortness of breath, cough and fever.

Fig 3. Estimated mean (A) Functional Assessment of Cancer Therapy–General (FACT-G), (B) EuroQol 5-Dimension (EQ-5D), and (C) EuroQol Visual Analog Scale (EQ-VAS) scores by treatment arm.



- FACT-G
 - higher scores with Sunitinib which were consistent with clinically meaningful differences.



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- EQ-5D Index
 - better with Sunitinib until cycle 5, d1
- EQ-VAS (overall health)
 - better with Sunitinib at all time points

Conclusions:

- Patients on Sunitinib have a significantly better QOL compared to those on Interferon.
- The positive results are largely due to between group differences (i.e.: Sunitinib vs. IFN) than within group differences (i.e.: improvement from baseline with Sunitinib).
- Some bias could be introduced given patients knew what treatment they were on.

Study commentary:

- Largest RCT in metastatic RCC comparing patient QOL in 2 different treatment arms (Sunitinib vs. IFN).
- Several different QOL questionnaires (validated disease specific and generic) were used, thus providing significant support for the conclusions.
- The primary endpoint (FKSI-DRS) focused on disease-related symptoms and not on treatment-related adverse events and, thus, it was useful to have the overall health status questionnaires as well (EQ-5D Index and EQ-VAS). But, it is still difficult to sort out treatment-related positive effects on the disease and treatment-related negative effects from toxicity.

Website link to source: www.jco.org (*J Clin Oncol* 2008; 26:3763-3769)