

Adverse Events of Antiretroviral drugs Clinician's Perspective

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AEs IN ART IN ZIMBABWE

- Few systematic studies
- Clearly common as seen in clinical trials and national programs
 - DART, A5175, A5208, HPTN 052, Others
- Anaemia-published (CROI 2005, Antiviral therapy 2006;11:741)
- Renal dysfunction in a TDF containing triple nuc regimen-published (IAC, Toronto 2006)
- Lipodystrophy & lipid changes-on-going study



Baseline characteristics



3316 participants (accrual completed Oct 2004)

- Sex 65% women
- Median age 37 years (IQR: 32-42)
- Median CD4 86 cells/mm³ (IQR: 31-140)
- WHO stage 23% WHO 4 56% WHO 3
- Median Hb 11.4 g/dl (IQR: 10.3-12.7)
- Anaemia 12% <9.5g/dl (grade 1)
- Median BMI 21.2 (IQR: 19.2-23.6)
- Median follow-up 48 weeks (IQR: 25-60, max: 96)

Data to 15 January 2005 (trial ongoing)



Incidence of anaemia



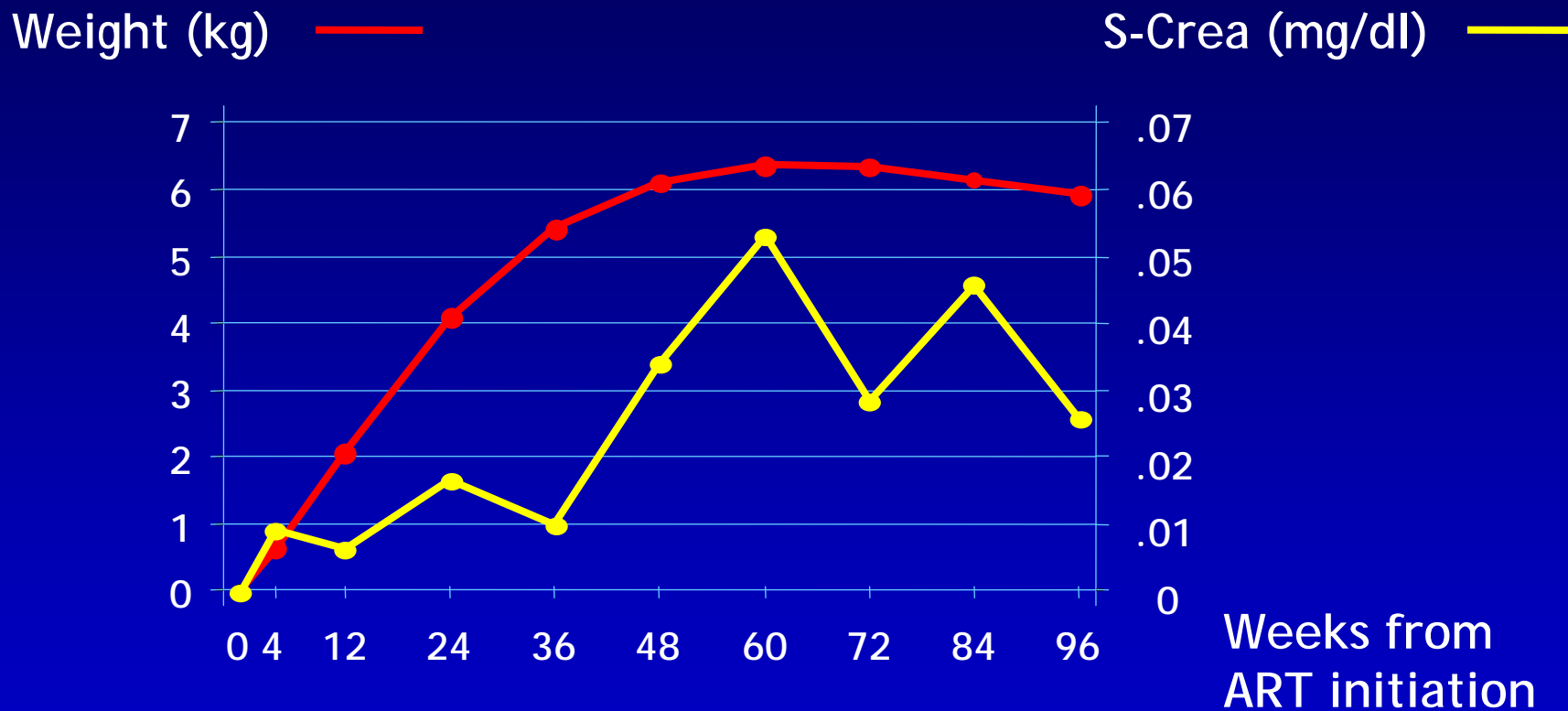
- Most severe new episode:

	n	%	cumulative
Grade 4 (<6.5 g/dl)	220	6.6 %	6.6 %
Grade 3	38	1.2 %	7.8 %
Grade 2	136	4.1 %	11.9 %
Grade 1	407	12.3 %	24.2 %

- 14 patients had >1 grade 4 episode



Weight and serum creatinine change after baseline

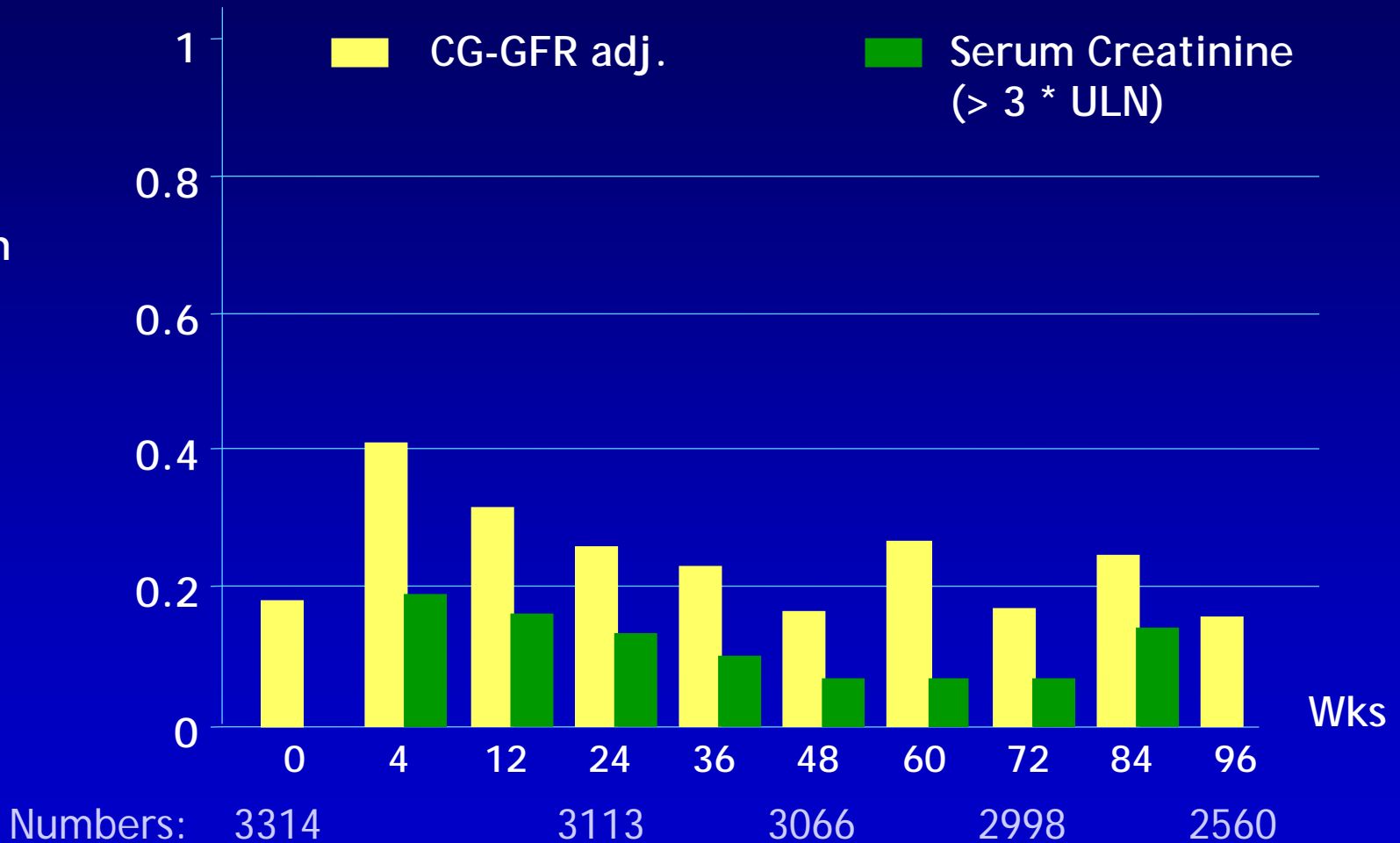


- Weight increase up to week 48 but stabilisation thereafter



Prevalence of impaired GFR* and raised S-Creatinine** (grade 3 or 4)

% with grade 3 or 4 reduction



* National Kidney Foundation; ** ACTG criteria

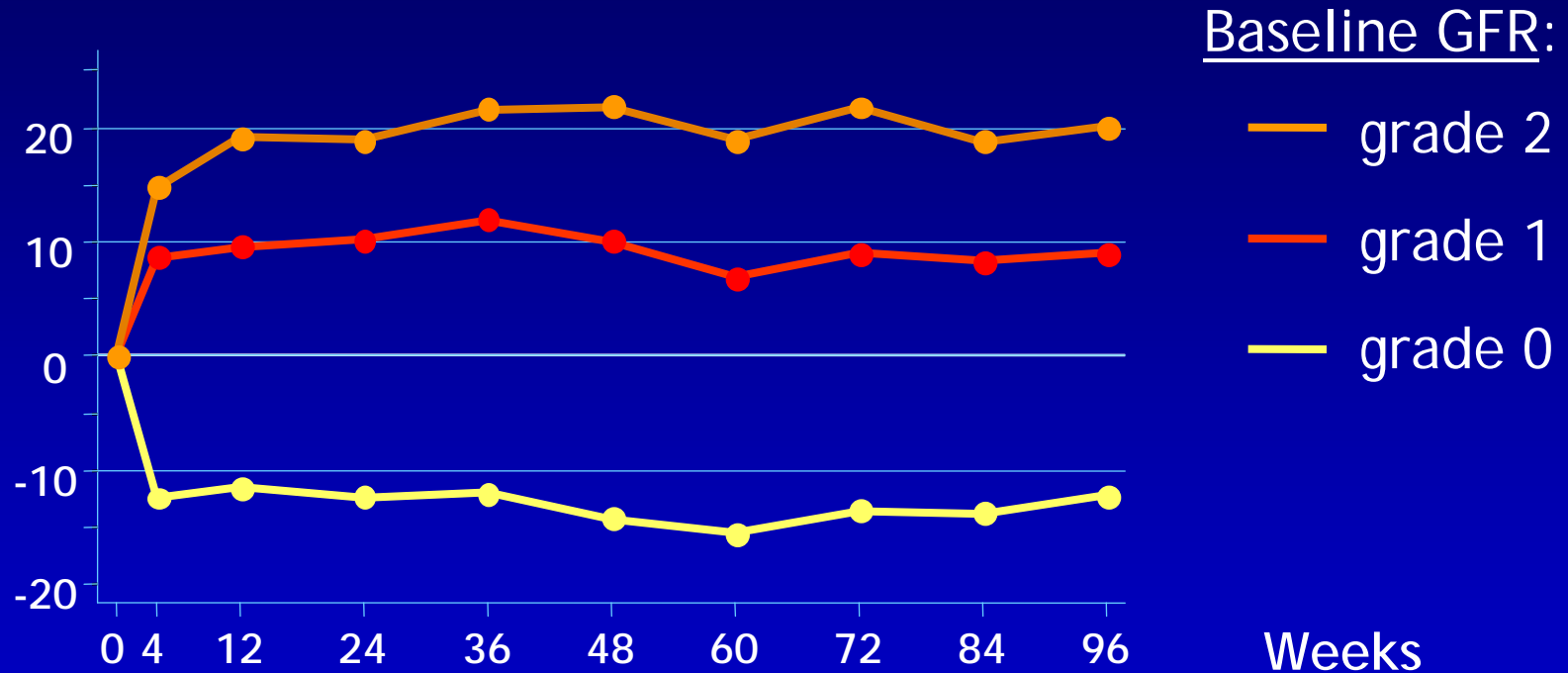


GFR over time by baseline GFR

- unadjusted analysis -



Mean GFR change (ml/min/1.73m²)



- Patients with mild renal impairment at baseline showed greater improvements than those without impairment
 - changes were within the normal range

Common AEs-Zim

- Common AEs well known and part of ART training
 - Nevirapine
 - Rash, hepatitis-less well know hypersensitivity
 - Efavirenz
 - CNS side effects
 - Stavudine
 - Peripheral neuropathy, metabolic AEs-lactic acidosis, lipodystrophy
 - Zidovudine
 - Anaemia, lactic acidosis, myositis
 - Tenofovir
 - Renal dysfunction
 - Protease Inhibitors
 - Lipid abnormalities, lipodystrophy

AEs-Issues

- Issues
 - Clinical trials
 - Reported to regulatory authorities according to standard definitions and guidelines eg DAIDS toxicity tables and MRCZ and MCAZ requirements
 - Programs
 - Reports according to national requirements MCAZ and National Drugs & Therapeutic Control Authority (NDTPAC)

AEs-Issues

- Knowledge
 - Clinical trials-excellent knowledge of DAIDS tables
 - Programs-lack of standard reporting
 - Coding
 - Definitions
 - Grading
 - Relatedness information

AEs

- Recognition-needs
 - Standardized reporting systems
 - Training
 - Opportunities for reporting
 - Routine pharmacovigilance
 - Targeted-clinical trials, program, etc
 - Accuracy ie full description
 - Concomitant medication including TB medicine, antimalarials, Cotrimoxazole
 - Traditional medicines/herbs
 - Over the counter medications-antiacids and H₂ antagonists

AEs

- Diagnosis
 - Presumptive/confirmed
 - Clinical descriptions/laboratory data
 - Symptomatic/asymptomatic
- Reporting
 - Emphasized in ART guidelines
 - Included in national formulaty



Thank you