

Evidence Based Health Care

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Definition

- Conscientious , explicit and judicious use of current best evidence in making decisions about the care of individual patients. Integrating individual clinical experience with the best available evidence from systematic research. (D. Sackett 1996)
- Integration of clinical expertise, patient values, and the best evidence into the decision making process for patient care
- Evidence does not make the decision; only helps. EBHC is often triggered by patient encounters which generate questions

Where is EBHC Practiced?

- Health System; population based
 - Formularies
 - Guidelines; critical pathways
 - Policy and procedures
- Individual patient care

The Challenge of Keeping Up

Journal	# of Articles	# (%) Meeting Criteria
NEJM	254	43 (16.9)
Ann Intern Med	246	33 (13.4)
JAMA	303	37 (12.2)
Arch Intern Med	262	27 (10.3)
BMJ	283	24 (8.5)
Lancet	410	30 (7.3)
	1,758	194

Haynes RB. Where's the meat in clinical journals? ACP Journal Club 1993;119:A22-3.

Steps in the EBHC Process

- The patient: clinical problem or question
- The question: formulate a question from the case
- Find the evidence
- Evaluate the evidence
- Apply the evidence: back to the patient
- Self-evaluation or follow-up

Targeted Approach to Learning

- Life-long, self-directed, problem-based learning around individual patients
 - Replaces or supplements routine literature review
 - Improves retention of knowledge
- Pragmatic process of using individual patient problems to expand knowledge

Why is EBHC Important

- 71 information searches for clinical questions from rounds
 - 37(52%) confirmed management decisions
 - 18(25%) lead to a new therapy or Dx test
 - 16(23%) corrected previous plan
 - Sackett D.
- Canadian Soc of Internal Medicine
 - Clinical experience 93%; Review articles 73%; colleagues 61%; textbooks 45%
 - 45% used EBHC related information sources

Pros and Cons

- Pros
 - Decisions based on strong evidence
 - Supports/augments clinical decisions
 - Provides new information not previously known
- Cons
 - Cook book medicine, down plays clinical experience
 - Literature doesn't apply to my patient
 - RDCT do not reflect real world
 - Takes too much time

Step 1

- The patient: a clinical problem or question arises out of care of the patient

Step 2: Formulate a Question



Case

- H.B. is a 26 yo male hispanic male who is HIV positive. He has been on therapy for 3 years consisting of Atripla once daily at night without any ADRs. He currently presents with a viral load of 10,000 copies/mL and a CD4 cell count of 400 cells/mL. At his last visit 3 months ago he had a non detectable viral load and a CD4 count of 450 cells/mL. A genotype reveals that he has a K103N and a M184V mutation.

Case continued

- The laboratory data reveals the following:
 - Electrolytes WNL
 - Creatinine 1.1 mg; CrCl estimated 95 ml/min
 - Total cholesterol 300; LDL 140
 - LFTs normal
- He has no other problems

Question

- What is the significance of the genotype?
- Can he continue with Atripla or does he need to switch to a different ART regimen?
- What regimen will be best for HB considering his desire to have something once daily.

Find the Evidence

Organization of the Biomedical Literature

- Tertiary
 - Reference books
 - Review articles
 - Guidelines
- Secondary
 - Indexing and abstracting services
- Primary
 - Original data—clinical trial, case reports, observational, etc.

Tertiary

- Summary of existing data
 - Advantages
 - Easy to review a lot of information
 - Peer reviewed
 - Comprehensive
 - Can be specialty focused
 - Disadvantages
 - Out of date quickly
 - May reflect bias of author
 - Errors occur
 - Data may be conflicting
 - Not always comprehensive or specific to your question
- Available in print and/or electronic versions

Clinical Practice Guidelines

- Tertiary source
 - Developed from primary literature
 - Usually compiled by expert panel
 - Easier to update if electronic
 - Need to determine when last update occurred
 - Usually give strength of evidence for recommendations
 - Usually disease specific

Sources of Primary Literature

- General (6 leading biomedical journals)
 - New England Journal of Medicine
 - JAMA
 - Annals of Internal Medicine
 - Archives of Internal Medicine
 - BMJ
 - Lancet

Sources of Primary Literature

- Specific
 - As with tertiary and secondary sources, each medical specialty has its own specialty journals
 - Examples
 - American Journal of Cardiology
 - Critical Care Medicine
 - Pediatrics
 - Journal of Clinical Oncology
 - Clinical Infectious Diseases
 - J of Acquired Immunodeficiency Syndrome

Sources of Primary Literature

- Pharmacy-specific
 - Annals of Pharmacotherapy
 - Pharmacotherapy
 - American Journal of Pharmaceutical Education
 - American Journal of Health-System Pharmacy
 - Journal of the American Pharmacists Association

Primary Literature

- Randomized double blind controlled clinical trial—"gold standard"
- Open label, randomized
- Non inferiority studies
 - Often used in antimicrobial studies
- Observational
 - Case report/series
 - Retrospective: cross sectional, cohort, case control

Primary Literature-cont

- Reviews
 - Review article
 - Systematic review
 - Meta-analysis
 - Clinical practice guideline

Randomized, Controlled Trials

- Patients who meet certain criteria are randomized to a treatment or control group and followed prospectively in time to see who develops the outcome of interest
- Strongest study design
 - Only one that can determine cause and effect
 - Why?

Randomized, Controlled Trials

- Since they are the strongest, they are most likely to change clinical practice.
- Even though they are the strongest, you must still critically evaluate the methods before you accept their conclusions.

Evaluation of Evidence

- Why do we need to do this?
 - Just because something is published does not mean it is true or of good quality
 - Over 20,000 biomedical journals published annually
 - 40 - 50% of articles have major flaws in design, analysis, and conclusions
 - Pharmacists need to evaluate literature to formulate opinions, solve therapeutic problems
 - Determining acceptable vs. fatal flaws

Study Design

- Three major study designs:
 - Descriptive
 - Case reports, case series, population studies
 - Observational
 - Case-control, cohort, cross-sectional studies
 - Experimental
 - Clinical trials
 - Superiority trials
 - Equivalency trials
 - Noninferiority trials

The Basics

- Journal
 - Reputable?
 - Is it peer-reviewed?
 - Is the article part of a supplement?
- Authors
 - Are the researchers qualified (degrees, well-published in the area)?
 - Is there a statistician involved?

The Basics

- Research site
 - Is it appropriate?
 - Does it have adequate resources and technology?
- Funding
 - Who funded the trial? Nonprofit organization? Pharmaceutical company?

The Basics

- Title
 - Is the title appropriate?
 - Should be brief, catch the attention of the reader, and describe the study sufficiently
 - Is the title unbiased?
 - “Greater microbiological and clinical cure rates with gatifloxacin versus levofloxacin in community acquired pneumonia - a randomized trial.”
 - Gatifloxacin versus levofloxacin for community acquired pneumonia - a randomized trial.”

The Basics

- Abstract - Is the abstract appropriate?
 - Allow reader to scan for interest
 - Abstract should describe:
 - Purpose, methods, results, conclusions
 - Structured Vs Unstructured
 - Do **NOT** rely on abstract for clinical decisions; they can be misleading, incomplete, or incorrect

Paper Organization

- Introduction
- Methods
- Results
- Discussion
- Conclusion
- References

Introduction

- Is the introduction representative of pertinent literature?
 - Should concisely summarize previous work in the area
 - Should equally present both sides of opposing views
 - Should cite literature other than only the study's investigators
- Does the introduction clearly state why the study was done?

Introduction

- Are the objective(s) clearly stated and appropriate?
 - Are the objectives specific?
 - Do they reflect the methodology?
 - Are the objectives obtainable within the scope of the study?
 - Are the number of objectives reasonable?
- Is the null hypothesis stated?

Introduction Objectives

- “The objective was to determine the efficacy of corticosteroids in patients with chronic lung disease.”
- “The objective was to determine whether corticosteroids improve results of spirometry or arterial blood gas levels, or both, in patients with chronic obstructive pulmonary disease and acute respiratory failure.”

Methods

- Things to consider:
 - Subjects
 - Intervention (treatment)
 - Measurements
 - Statistical Analysis



Methods--Subjects

- How many subjects were studied?
- How were subjects recruited?
 - Are they representative of the population?
 - General practice vs. specialized referral practice
 - Multi-center vs. single-center study
 - Were subjects randomly selected?
- Ethical issues:
 - Was the protocol approved by an investigational review board? Did the subjects give informed consent?

Methods--Subjects

- Were the inclusion criteria clearly stated and appropriate?
 - Subjects and disease should be clearly defined and criteria should be objective
- Were the exclusion criteria clearly stated and appropriate? Anything missing?
- Inclusion / exclusion criteria determine external validity (generalizability)

Inclusion/Exclusion Criteria

- Inclusion
 - The study enrolled over 300 adult patients with high blood pressure
 - The study enrolled 325 patients aged 18 to 65 years old with a systolic blood pressure ≥ 140 mmHg and a diastolic blood pressure ≥ 90 mmHg based on an average of three measurements taken 3 weeks apart
- Exclusion
 - The study excluded patients with renal dysfunction
 - The study excluded patients with renal dysfunction defined as serum creatinine ≥ 1.5 g/dL or CrCl < 50 ml/hr

Methods--Intervention

- Was the study design appropriate for the hypothesis and objectives?
- Was the design parallel or cross-over?
 - Parallel - subjects only receive one treatment
 - Cross-over - subjects receive all treatments
 - Minimizes patient variability
 - Can be used in chronic diseases, but not acute diseases
 - Requires an adequate wash-out period

Methods--Intervention

- Were subjects randomly assigned to treatment groups?
 - Was the procedure truly random?
- Were the controls appropriate?
 - Placebo control
 - Active control (preferred)
 - Historical control (open-label)

Methods--Intervention

- Was the study blinded?
 - Single-blinded (investigator- or subject-blinded)
 - Double-blinded (both investigator and subjects)
 - Unblinded
 - Less bias introduced if measurements are objective
 - Unblinded studies should attempt to use outside blinded evaluators

Methods--Intervention

- Were the treatment regimens appropriate?
 - Specifics regarding treatment should be clear
 - Dose, frequency, route of administration, duration
 - Active controls should use standard treatment
 - Dosing should be appropriate

Measurements

- Were the outcome variables appropriate?
 - Are they objective, practical, and clearly defined?
 - Are they clinically relevant?
 - Were surrogate endpoints used?
 - Ex: Blood pressure vs. vascular complications *or* HIV viral load vs. mortality
 - Surrogate endpoints should only be used when they have been correlated with clinical endpoints

Measurements

- Were measurements of endpoints appropriate?
 - “Gold standard” methods should be used
 - If subjective, should demonstrate validity
- Who took the measurements?
 - If multicenter, were measurements standardized?
 - If multiple observers used, did the measurements correlate?

Measurements

- Was compliance assessed?
 - Pill counts, urine/serum drug concentrations, computerized prescription vials
 - Were concomitant treatment methods recorded?
- Was the duration of the trial sufficient?
 - Consider for both treatment effect and tolerability
- Are there confounding variables not being measured?

Statistical Analysis

- Was a power-analysis done?
 - What power was used; what p-value is significant?
 - Did the authors anticipate drop-outs?
 - How many patients were required for statistical conclusions to be made?
- Were statistical tests appropriate?
 - How many groups?
 - What type of data (nominal, ordinal, interval, or ratio)?
 - Is the data parametric or nonparametric?
 - Were multiple statistical tests used on the same data?

Statistical Analysis

- Were statistical tests one-tailed or two-tailed?
 - Two-tailed test requires a stronger relationship to achieve statistical significance
- What kind of analysis was done?
 - Per-protocol
 - Analyzes patients who adequately complete study
 - Intention-to-treat
 - Analyzes all subjects including those who die or drop out of the study

Results

- Were the groups equally matched?
 - If not, are the differences discussed and are they clinically meaningful?
- Were all results presented?
 - Were the results presented clearly?
 - P-values and confidence intervals should be provided
 - Standard deviation vs. standard error of the mean (SEM)
 - Were there any table or graph distortions?
 - Axes should be labeled and units should have equal intervals

Results

- Were all drop-outs accounted for?
- Were subgroup analyses done?
 - Were there enough patients in each subgroup to make statistical conclusions?
 - Did the authors state they would do subgroup analyses in the methodology?
- Were differences statistically significant and/or clinically significant?

Discussion and Conclusion

- Were valid conclusions drawn?
 - Were they based on the objectives, methods, and results?
- Did the authors discuss the trial's limitations?
 - Should explain how the limitations might affect the results
- Did the authors compare and contrast the results to previously conducted research?

References

- Was the trial referenced with appropriate literature?
 - Should use pertinent, current articles from reputable journals
 - Should avoid excessively citing their own research

Additional Things to Consider

- Type I and Type II Errors
 - Type I - rejecting the null hypothesis when it is true (a false-positive result)
 - Results may be due to chance
 - Probability is equal to alpha or the level of significance
 - Type II - accepting the null hypothesis when it is not true (a false-negative result)
 - Usually the result of inadequate sample size
 - Probability is equal to beta

Additional Things to Consider

- Applying the study results to clinical practice
 - Are the results valid (internal validity)?
 - Are results due to chance or confounding factor(s)?
 - To whom can the results be applied (external validity)? Is it appropriate for my patient.
 - Is the intervention practical and would it be acceptable to patients?
 - Are the benefits worth the associated risks and costs?

Superiority Trials

- Null hypothesis
 - Drug A and B are equal; if statistically different then reject null hypothesis
- Trying to show better or inferior to control
- Use ITT in favor or “per-protocol” analysis
 - Analysis of all those randomized
 - More real life
 - Decreases chance of Type I error

Equivalency Trials

- Trying to show that two are the same
- Margin of efficacy for evaluating new agent
 - Set a margin where new agent is expected to perform

Noninferiority Trials

- New agent compared to standard active agent
- Goal is to basically show equivalency
- Null hypothesis is opposite of superiority
 - Drug A is worse than drug B
 - Reject Null if Drug A is Same as Drug B i.e. noninferior
- Only a one sided (one tail) argument when others are two sided (two tail)

Noninferiority trials

- Antimicrobials
- Most antiretroviral trials involving new agents or regimens
- Design used when placebo is unethical
- Assumes comparator agent is effective
- Difficult to design, conduct and interpret
- Need to evaluate carefully
- Primer: Kaul S, Diamond GA. Ann Intern Med.2006;145:62-9

What HAART is Appropriate for
HB?

Preferred Agents for Naïve Pts

- NNRT- based regimen
 - Efavirenz: do not use during pregnancy; use with caution in pts with psychiatric disease*
- PI-based regimen (boosted)
 - Atazanavir + ritonavir once daily*
 - Darunavir + ritonavir once daily*
- INRTI-based regimen
 - Raltegravir*
- Preferred for pregnant women
 - Lopinavir/ritonavir + zidovudine/lamivudine

*plus tenofovir and emtricitabine for NRTI component

TITAN: Virologic Outcomes With DRV/RTV vs LPV/RTV in Tx-Experienced Patients

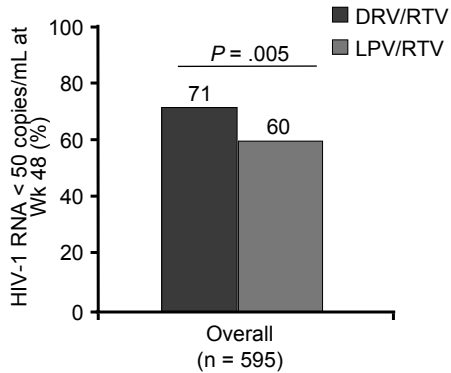
- DRV- and LPV-naïve patients with HIV-1 RNA > 1000 c/mL and on current regimen for ≥ 12 wks randomized to
 - DRV/RTV 600/100 mg BID plus OBR or
 - LPV/RTV 400/100 mg BID plus OBR

Previous ARV Experience, %	DRV/RTV (n = 440)	LPV/RTV (n = 443)
≥ 4 NRTIs	52	51
≥ 1 NNRTI	76	77
0 PI	32	31
1 PI	36	39
≥ 2 PIs	32	30
3-class experienced	46	46

Madruca JV, et al. Lancet. 2007;370:49-58.

TITAN: Virologic Outcomes With DRV/RTV vs LPV/RTV in Tx-Experienced Patients

- DRV/RTV superior to LPV/RTV in rates of
 - HIV-1 RNA < 400 copies/mL at Wk 48 (primary endpoint)^[1]
 - HIV-1 RNA < 50 copies/mL at Wk 48^[1]
 - HIV-1 RNA < 400 copies/mL at Wk 96^[2]
- All analyses ITT-TLOVR



1. Madruga JV, et al. Lancet. 2007;370:49-58. 2. De Meyer S, et al. Glasgow 2008. Abstract O424.

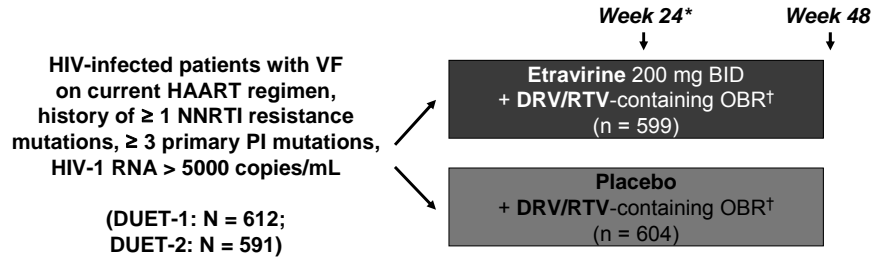
NRTI + 3TC/FTC + Boosted PI Effective Second-Line Regimen in Pts With M184V

- British Columbia HIV Drug Treatment Program, 2000-2006
- Pts with M184V ± NNRTI RAMs but no PI or other NRTI RAMs (N = 117)
- No significant difference in likelihood of HIV-1 RNA suppression between 3 types of second-line regimen
 - No advantage from including an additional active agent or sparing 3TC/FTC

Second-Line Regimen	HR, Time to Virologic Suppression (95% CI)
3TC/FTC + NRTI + boosted PI	Ref
3TC/FTC + NRTI + boosted PI + additional active agent(s)	1.09 (0.60-1.96)
3TC/FTC-sparing NRTIs + boosted PI ± additional active agent(s)	0.61 (0.37-1.03)

Hull M, et al. ICAAC 2009. Abstract H-916.

DUET-1 and -2: Etravirine + DRV/RTV-Containing OBR Phase III Trials

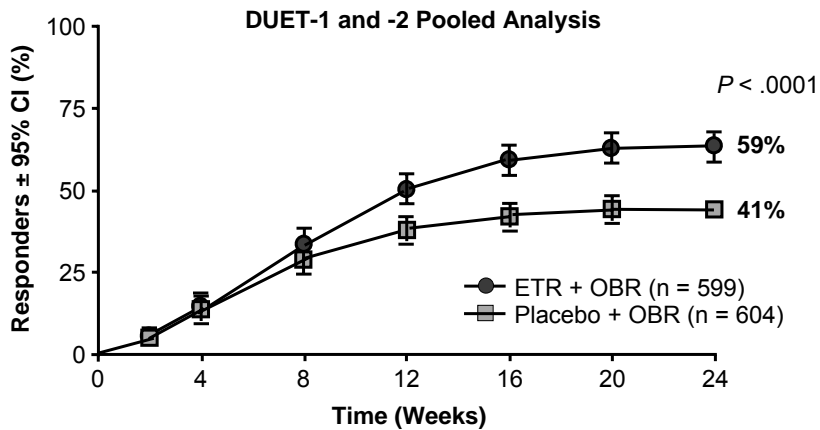


*Planned Week 24 analysis: primary endpoint HIV-1 RNA < 50 copies/mL (TLOVR).

[†]Investigator-selected OBR to consist of DRV/RTV (600/100 mg/mL) + ≥ 2 NRTIs \pm ENF.

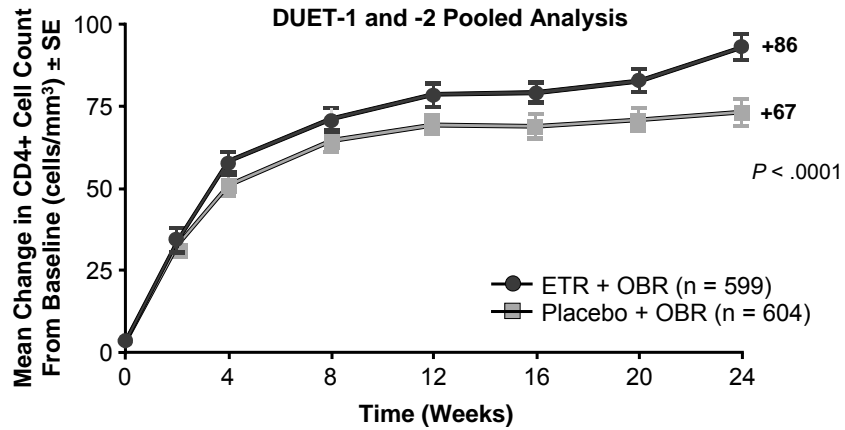
Madruza JV, et al. Lancet. 2007;370:29-38. Lazzarin A, et al. Lancet. 2007;370:39-48.
Mills A, et al. IAS 2007. Abstract WESS204.1. Katlama C, et al. IAS 2007. Abstract WESS204.2. Cahn P, et al. ICAAC 2007. Abstract H-717.

DUET-1 and -2: Patients With VL < 50 c/mL at Week 24 (ITT TLOVR)



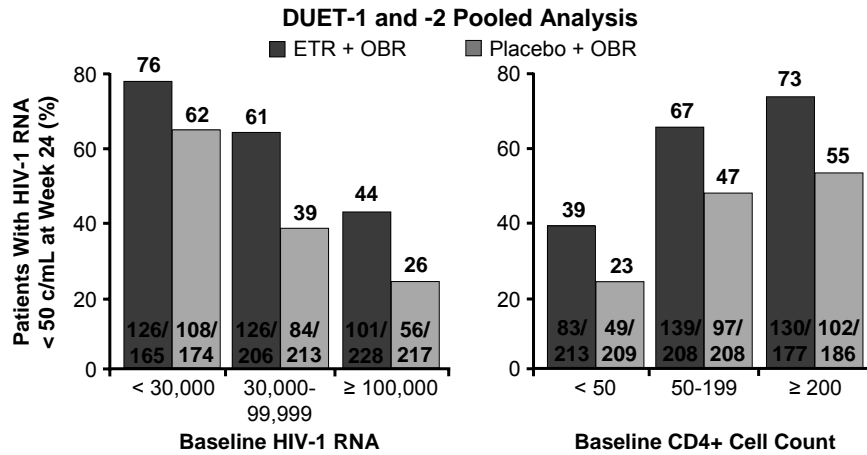
Cahn P, et al. ICAAC 2007. Abstract H-717.

DUET-1 and -2: Change in CD4+ Cell Count From Baseline (ITT NC = F)



Cahn P, et al. ICAAC 2007. Abstract H-717.

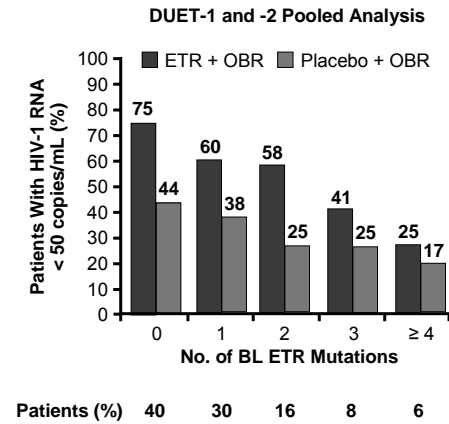
DUET-1 and -2: Response (< 50 c/mL) According to BL CD4+ and VL



Cahn P, et al. ICAAC 2007. Abstract H-717.

DUET-1 and -2: BL ETR Mutations and Virologic Response at Week 24

- 13 mutations associated with ETR resistance
 - V90I - A98G
 - L100I - K101E/P
 - V106I - V179D/F
 - Y181C/I/V - G190A/S
- Presence of ≥ 3 ETR mutations associated with response similar to overall placebo + OBR response
 - 70% of patients had 0 or 1 ETR resistance mutations at BL
 - 14% of patients had ≥ 3 ETR resistance mutations at BL



Cahn P, et al. ICAAC 2007. Abstract H-717.

DUET-1 and -2: Any Grade Adverse Events at Week 24

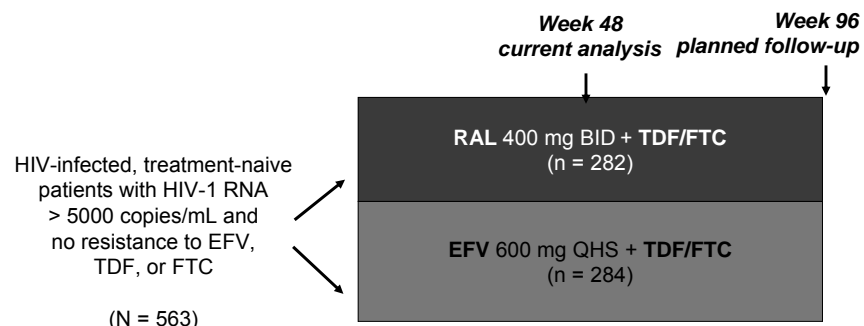
Adverse Events Through Week 24, %	Etravirine (n = 599)	Placebo (n = 604)
Adverse event of any grade	93	93
Rash (all types)	17*	9
Diarrhea	15	20
Nausea	14	11
Headache	9	12
Neurologic disorders	15	19
Psychiatric disorders	13	15
Hepatic adverse events	5	5

Cahn P, et al. ICAAC 2007. Abstract H-717.

Summary of Etravirine Clinical Data

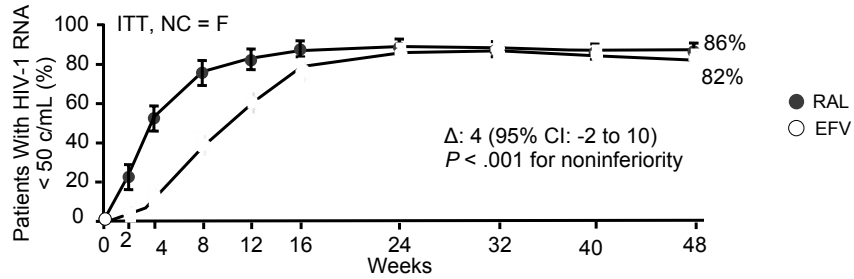
- In treatment-experienced patients, including those with NNRTI-resistant virus, ETR superior to placebo when each were combined with a DRV/RTV-containing OBR
 - 59% of patients achieved VL < 50 copies/mL with etravirine + DRV/RTV-based OBR at Week 24
 - Other than rash, incidence of AEs and lab abnormalities similar to placebo
- 13 etravirine-resistance associated mutations identified
 - K103N not associated with etravirine resistance
- Presence of ≥ 3 etravirine resistance mutations associated with substantially decreased response
- Only 14% of DUET patients had ≥ 3 etravirine mutations
- TMC125-C227 reinforces importance of combining ETR (like all other drugs) with at least 1 other active drug

STARTMRK Phase III: RAL vs EFV in Treatment-Naive Patients



- Primary endpoint: HIV-1 RNA < 50 copies/mL, safety, and tolerability at Wk 48
- Secondary endpoint: CD4+ cell count
- 53% of patients had HIV-1 RNA > 10⁵ copies/mL; 47% of patients had CD4+ cell counts ≤ 200 cells/mm³ at baseline

STARTMRK: Virologic and Immunologic Efficacy at Week 48

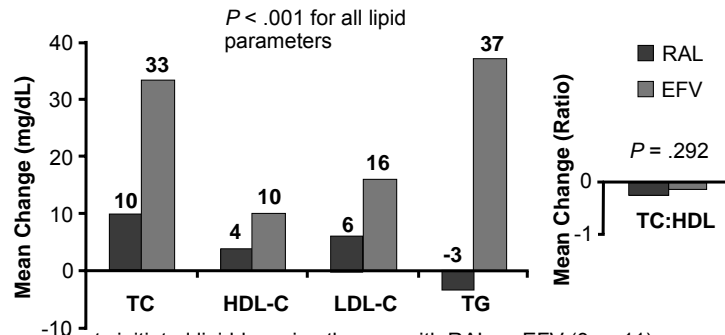


RAL n =	281	279	281	279	281	279	278	280	280
EFV n =	282	282	282	282	281	282	280	281	281

- Significantly shorter time to virologic response with RAL vs EFV ($P < .001$)
- Significantly greater CD4+ cell count increase with RAL vs EFV
 - +189 vs +163 cells/mm³; Δ: 26 cells/mm³ (95% CI: 4-47)

Lennox J, et al. ICAAC/IDSA 2008. Abstract 896a. Adapted with permission of Merck & Co., Inc., Whitehouse Station, New Jersey, USA, Copyright © 2008 Merck & Co., Inc., All Rights Reserved.

STARTMRK: Lipid Changes From BL to Week 48



- Fewer patients initiated lipid-lowering therapy with RAL vs EFV (3 vs 11)
 - 4 patients in each arm increased lipid-lowering therapy
- Greater increases in all lipid parameters including HDL in EFV arm; no overall difference in TC:HDL ratio

Lennox J, et al. ICAAC/IDSA 2008. Abstract 896a. Adapted with permission of Merck & Co., Inc., Whitehouse Station, New Jersey, USA, Copyright © 2008 Merck & Co., Inc., All Rights Reserved.

Recommendations: Patients With Initial NNRTI Failure

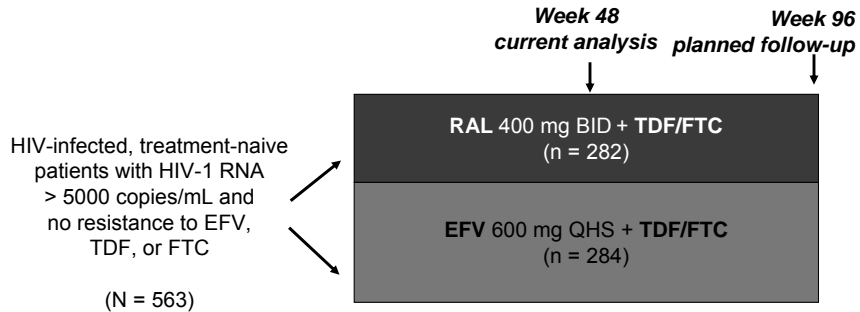
- Assess and address cause(s) of failure
- Boosted PI regimens well studied, expected to be effective
- Few comparative data in initial failure
- Backbone: 2 NRTIs likely sufficient if no NRTI resistance or M184V alone
- If more complex NRTI mutations, combinations of novel agents and boosted PIs may be preferable
- Maraviroc may also be considered; needs trophile assay first.

Strategies to Avoid/Use With Caution With Compromised NRTIs

- 2 NRTIs + ETR
 - TMC125-C227 study demonstrated ETR inferior to PI in patients with first-line NRTI + NNRTI failure and resistance^[1]
- 2 NRTIs + RAL
 - SWITCHMRK suggests previous virologic failure (NRTI resistance) associated with increased risk of rebound on 2 NRTIs + RAL^[2]

1. Ruxrungtham K, et al. HIV Med. 2008;9:883-896.
2. Eron J, et al. Lancet. 2010;375:396-407.

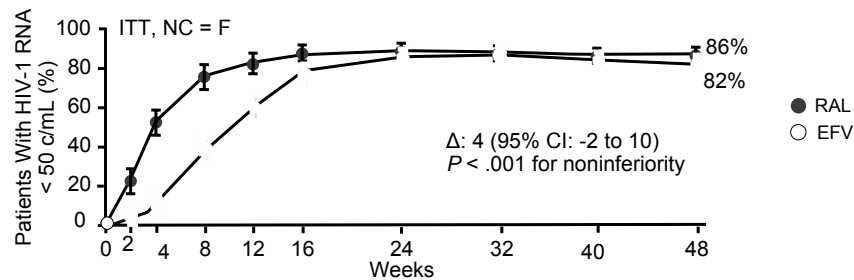
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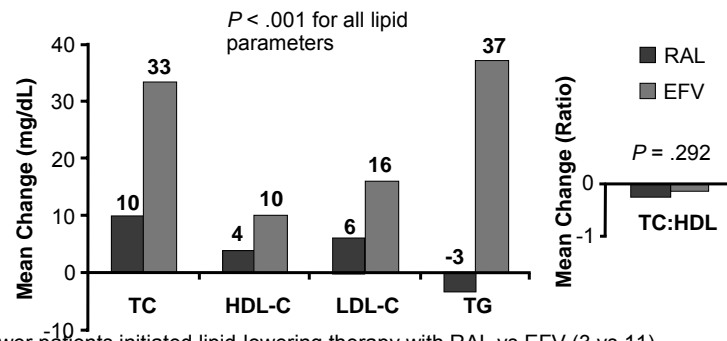


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STARTMRK: Lipid Changes From BL to Week

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Return to the Patient

Case

- H.B. is a 26 yo male hispanic male who is HIV positive. He has been on therapy for 3 years consisting of Atripla once daily at night without any ADRs. He currently presents with a viral load of 10,000 copies/mL and a CD4 cell count of 400 cells/mL. At his last visit 3 months ago he had a non detectable viral load and a CD4 count of 450 cells/mL. A genotype reveals that he has a K103N and a M184V mutation.

Case continued

- The laboratory data reveals the following:
 - Electrolytes WNL
 - Creatinine 1.1 mg; CrCl estimated 95 ml/min
 - Total cholesterol 300; LDL 140
 - LFTs normal
- He has no other problems
- Would like a daily dose regimen
 - Adherence may be reason for failure

Suggestions for HB

- Daily dosing options:
 - Darunavir/r + tenofovir + emtricitabine
 - Two active agents; FTC may boost TDF
 - LPV/r + tenofovir + emtricitabine
 - Not recommended for advanced patients
 - Atazanavir/r + tenofovir + emtricitabine
- Twice daily dosing
 - DRV/r + TDF + FTC + etravirine
 - Three active agents

Suggestions for HB

- Raltegravir + tenofovir + emtricitabine

Other types of Evidence

Observational

- Observational
 - Case report/series
 - Provides lowest level evidence from scientific perspective
 - Can be helpful especially for ADRs
 - Retrospective: cross sectional, cohort, case control
 - Cannot show cause and effect relationship
 - Can provide good information for population based decisions
 - Often leads to prospective controlled studies

Electronic/Web Based

- Government sites
 - FDA, CDC, NIH, DHHS, AHRQ
- National organizations
- Commercial sites
 - Medscape—free to health care professionals
 - Micromedex
 - CRL-online
 - Pharmacist letter

Electron/Web Based

- Search engines
 - Google, yahoo, etc
 - Pubmed
 - Medline

Evaluation of Web Based Information

- Who maintains the site?
- Medical professionals / societies; government sites; private companies; individuals
Who wrote the information?
- When was the site last updated?
- How is the site funded?
- Is there a formal review mechanism for the information?

Evaluation of Web Based Information

- Does the site provide clinically or scientifically based evidence to support it's statements?
- Is there a disclaimer that this is general information?
- Does the site ensure patient confidentiality?
- Can you contact the host?

Example Application of Applying Evidence to Clinical Decision Making

Case: Strep Throat

- Bobby is a 5 yo male in for fever and sore throat for several days. He has a positive strep test and you want to start therapy. Standard treatment is penicillin 3 times daily. You are concerned about cost and adherence. You had heard that one daily dose of amoxicillin is just as good. You want to review the literature on this to see about changing.

Construct the clinical question

- In children with strep throat, is amoxicillin as effective as penicillin for relief of symptoms?
- What is the best treatment for relieving symptoms of a sore throat?
- Is amoxicillin better than penicillin for young children?

Conduct a literature search

- Search pharyngitis
- Search Streptococcus
- Search amoxicillin
- Search penicillin
 - Search all four in combined search to limit articles and limit to RCT and children 0-18
 - Should get less than 50 articles

Relevant Article from Search

- Feder HM, et al. Once-daily therapy for Streptococcal pharyngitis with amoxicillin. *Pediatrics* 1999;103:47-51
 - Randomized double blind trial
 - No difference between groups at 18-24 hour follow-up visit
 - No difference in rate of symptom resolution
 - Adverse effects were similar
 - Once daily dosing is as effective as TID penicillin dosing over 10 days
 - Study was underpowered and may have type II error; failure to show a difference due to too few subjects. There were less than 100 in each arm and 353 were needed for 80% power.

Back to the Patient

- Is this article relevant to Bobby?
- Would you recommend amoxicillin once daily over penicillin three times daily?

Conclusions

- We are a science based profession
- Clinical decisions based on evidence lends credibility and improves patient care
- Not all clinical questions can be answered directly with evidence
- Evaluation and extrapolation is often key
- The ultimate decision in the end is based on what is best for the patient

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