Should RCT Search Filters Account For The Phases Of Clinical Trials In Addition To Study Design?

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The CONSORT statement says

Table 1: CONSORT 2010 checklist of information to include when reporting a randomised trial*

Section/Topic	Item No	Checklist item	Reported on page No
Title and abstract			
	1a	Identification as a randomised trial in the title	
	1b	Structured summary of trial design, methods, results, and conclusions (for specific guidance see CONSORT for abstracts [21,31])	

which means study design search filters *should* work

Royle and Waugh 'Rapid and Sensitive' Search filter (2007)

1. randomized controlled trial.pt.

Box 6.4.c: Cochrane Highly Sensitive Search Strategy for identifying randomized trials in MEDLINE: sensitivity-maximizing version (2008 revision); Ovid format

1. randomized controlled trial.pt.
2. controlled clinical trial.pt.
3. randomized.ab.
4. placebo.ab.
5. drug therapy.fs.
6. randomly.ab.
7. trial.ab.
8. groups.ab.
9. 1 or 2 or 3 or 4 or 5 or 6 or 7 or 8
10. exp animals/ not humans.sh.
11. 9 not 10

by way of introduction

Fluorouracil, Leucovorin, and Irinotecan Plus Cetuximab Treatment and *RAS* Mutations in Colorectal Cancer

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Published online ahead of print at www.jco.org on January 20, 2015.

Processed as a Rapid Communication manuscript.

Supported by Merck KGaA, which also funded medical writing services.

Presented in part at the 50th Annual Meeting of the American Society of Clinical Oncology, Chicago, IL, May 30-June 3, 2014, and European Society for Medical Oncology 16th World Congress on Gastrointestinal Cancer, Barcelona, Spain, June 25-28, 2014.

A B S T R A C T

Purpose

The phase III CRYSTAL study …

leucovorin, irvival, and 2) wild-type metastatic colorectal cancer (mCRC). Outcome was reassessed in subgroups defined by extended *RAS* mutation testing.

Patients and Methods

Existing DNA samples from *KRAS* exon 2 wild-type tumors from CRYSTAL study patients were reanalyzed for other *RAS* mutations in four additional *KRAS* codons (exons 3 and 4) and six *NRAS* codons (exons 2, 3, and 4) using beads, emulsion, amplification, and magnetics technology. No tissue microdissection was performed. A ≥ 5% mutant allele cutoff was used to call mutations.

Results

Mutation status was evaluable in 430 (64.6%) of 666 patients with *KRAS* exon 2 wild-type tumors. Other *RAS* mutations were detected in 63 (14.7%) of 430 patients. In those with *RAS* wild-type tumors, a significant benefit across all efficacy end points was associated with the addition of cetuximab to FOLFIRI. In patients with other *RAS* tumor mutations, no difference in efficacy outcomes between treatment groups was seen. The safety profile in *RAS* subgroups was similar and in line with expectations.

Conclusion

In the first-line treatment of mCRC, patients with *RAS* wild-type tumors derived a significant benefit from the addition of cetuximab to FOLFIRI; patients with *RAS* tumor mutations did not. Molecular testing of tumors for all activating *RAS* mutations is essential before considering anti–epidermal growth factor receptor therapy, thereby allowing the further tailoring of cetuximab administration to maximize patient benefit.

our case study

Database(s): Ovid MEDLINE(R) 1946 to Present Search Strategy:	Database: Ovid MEDLINE(R) In-Process & Other Non-Indexed Citations and Ovid MEDLINE(R) <1946 to Present> Search Strategy:
# Searches Results	# Searches Results
1 randomized controlled trial.pt. (409861)	1 randomized controlled trial.pt. (414089)
2 clinical trial, phase iii/ (10790)	2 controlled clinical trial.pt. (90577)
3 ("Phase 3" or "phase3" or "phase III" or P3 or "PIII").ti,ab,kw. (48056)	3 randomized.ab. (343788)
4 2 or 3 (52117)	4 placebo.ab. (168948)
5 4 not 1 (40874)	5 drug therapy.fs. (1847843)
6 limit 5 to yr=”2015” (3800)	6 randomly.ab. (247163)
	7 trial.ab. (355913)
	8 groups.ab. (1543475)
	9 1 or 2 or 3 or 4 or 5 or 6 or 7 or 8 (3719546)
	10 clinical trial, phase iii/ (11028)
	11 ("Phase 3" or "phase3" or "phase III" or P3 or "PIII").ti,ab,kw. (48665)
	12 10 or 11 (52814)
	13 12 not 9 (21244)
	14 limit 13 to yr="2015 -Current" (1846)

Inclusion Criteria:

any randomised trial

(any population, intervention or outcomes)

Royle and Waugh Rapid and Sensitive Filter

3800 unique studies were identified in MEDLINE (OVID). these were single screened

(work is on-going) but, in an early sample of 200 studies, we uniquely identified 12 RCTs using our filter

these studies had been incorrectly indexed by publication type

Cochrane Highly Sensitive Search Strategy (HSSS)

1846 studies were uniquely identified in MEDLINE (OVID). these were single screened

14 RCTs were uniquely identified using our filter

the primary reason these studies were missed by the HSSS is because they lacked an abstract. The HSSS for OVID only searches free-text on abstract

5 erratum, corrections or retractions were also missed by the HSSS. 2 of these were not in EMBASE (OVID) or CENTRAL

some things to bear in mind

the Royle and Waugh filter is a rapid and pragmatic study design filter. It aims to identify the majority of trials as efficiently as possible

the HSSS aims to maximise sensitivity and so we would anticipate lower relative inclusion from our filter

both filters focus on identifying studies in bibliographic databases. The process of study identification includes supplementary search methods that may identify missed studies later on in the review time-line

implications

the effect of missing studies

our early findings suggest that including search terms for the phase of the RCT could improve study identification of randomised trials in bibliographic databases: improving the speed of study identification

including search terms for the phase of RCTs increases sensitivity (also increasing N to screen)

integrating these search terms into well known study design filters is easy

the end

Search Strategy:

1 ("Phase 3" or "phase3" or "phase III" or P3 or "PIII").ti,ab,kw.
2 *Clinical Trial, Phase III/
3 ("Phase 2" or "phase2" or "phase II" or P2 or "PII").ti,ab,kw.
4 *Clinical Trial, Phase II/

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Please cite this:

Cooper, C., Briscoe, S., & Crathorne, L., (2016) *Should RCT Search Filters Account For The Phases Of Clinical Trials In Addition To Study Design?* Paper presented at HTAi, Tokyo, Japan.

Slides are freely available at:

http://medicine.exeter.ac.uk/esmi/workstreams/informationscience/our_research/