Oklahoma State University - Center of Health Sciences/Department of Student Research

Assessing Risk/Benefit Profile of Lapatinib in Clinical Trials

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OBJECTIVES

Our study analyzed all oncologic clinical trials using the drug lapatinib to create a risk/benefit profile of this drug.

INTRODUCTION

Drug manufacturers allocate large amounts of time and capital to the development of novel chemotherapies. To make up these costs, companies may seek to repurpose their medications to extended indications via clinical trials. Thus, a portfolio should be created to better understand the risk/benefit.

METHODS

- We conducted a search for studies of lapatinib treating solid cancers in Pubmed, Embase, Cochrane CENTRAL, and ClinicalTrials.gov.
- Eligible articles were required to be adult clinical trials, use RECIST criteria, be published in English, and involve solid tumors.
- Screening and data collection were completed in a masked, duplicate manner.
- We extracted trial characteristics, median progression-free survival (PFS) and overall survival (OS) in months, adverse event rates, and objective response rate for each study.
- We labeled studies positive, negative, or indeterminate based on their pre-specified endpoints and tolerability.

RESULTS

Figure 1: Flow Diagram

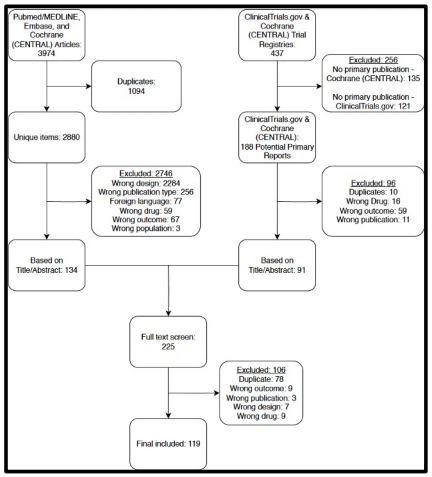

Figure 1. Flow diagram for study inclusion. One hundred and nineteen studies were included in analysis.

Figure 2: AER vs the cumulative ORR

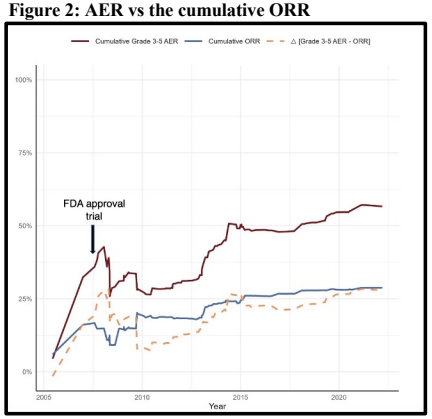

Figure 2: AER for each trial vs the cumulative ORR per each trial plotted per publication date. Δ[Grade 3-5 AER-ORR] is the absolute difference between cumulative AER and ORR.

Table 1: Overall Trial Characteristics and Outcomes by Indication

Indication	# of Trials	# of Randomized Trials (n, (%))	# of Participants	# of Males	# of Females	# of GRADE 3 - 5 Events	Median Age	Median PFS (months)	Median OS (months)	Median Partial Response Rate*	Median Complete Response Rate	Median ORR
Breast Cancer	75	30 (40.0%)	9789	13	9776	5189	53.5	5.9	23.2	28.7%	0	31.3%
Cervical Cancer	1	1 (100.0%)	228	0	228	143	49.3	4.4	11.2	6.0%	1.3%	7.3%
Colorectal Cancer	2	0 (0.0%)	56	39	17	21	62.5	3.7	9.2	13.0%	1.9%	14.8%
Endometrial Cancer	1	0 (0.0%)	30	0	30	15	-	1.8	7.3	3.3%	0.0%	3.3%
Esophagogastric Cancer	3	1 (33.3%)	59	46	13	45	61.9	2.5	10.7	13.9%	0.0%	13.9%
Gastric Cancer	4	2 (50.0%)	400	258	75	627	62	5.5	9.5	19.7%	0.0%	19.7%
Hepatocellular Carcinomas	1	0 (0.0%)	26	18	8	3	58	1.9	12.6	0.0%	0.0%	0.0%
Multiple Indications	22	1 (4.5%)	1465	779	686	651	60	2.3	8.4	6.8%	0.00%	8.0%
Non-Small Cell Lung Cancer	2	1 (50.0%)	149	71	78	38	66	3.1	14.6	1.5%	0.0%	1.5%
Ovarian Carcinoma	1	0 (0.0%)	12	0	12	9	67	-	-	27.3%	0.0%	27.3%
Pancreatic Cancer	1	0 (0.0%)	17	13	4	5	-	2.6	5.2	0.0%	0.0%	0.0%
Pancreaticobiliary Cancer	1	0 (0.0%)	25	13	12	24	63	-	11.0	16.7%	0.0%	16.7%
Renal Cell Carcinoma	1	1 (100.0%)	416	305	111	20	61.5	-	11.3	1.0%	0.0%	1.0%
Salivary Gland Cancer	1	0 (0.0%)	39	28	11	21	58	2.8	13.8	0.0%	0.0%	0.0%
Squamous Cell Carcinoma	2	1 (50.0%)	138	111	27	98	58	-	-	12.5%	4.2%	16.7%
Transitional Cell Carcinoma	1	0 (0.0%)	59	42	17	13	64	-	4.5	2.7%	0.0%	2.7%
Totals/Medians	119	38 (31.9%)	12908	1736	11105	6922	55	5	16.1	27.4%	1.3%	30.7%

*Response rate median calculations for those indications using RECIST or mRECIST only

Figure 3: AERO Diagram

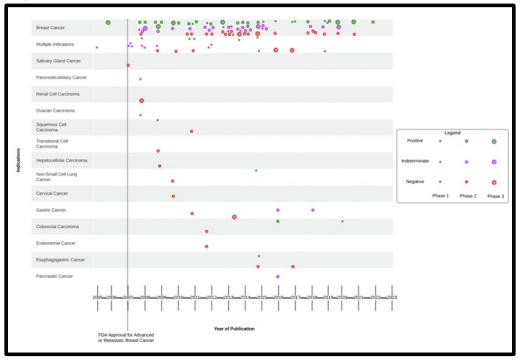

Figure 3: AERO diagram for lapatinib clinical trials.

CONCLUSION

Lapatinib showed effectiveness for its approved indication as a combination therapy while showing limited benefit in off-label indications. The risk-benefit analysis of lapatinib confirmed its efficacy. Although efficacious in breast cancer, the adverse event rates increased across clinical trials. Future trials using lapatinib should evaluate the risk-benefit profile before utilizing this measure.

REFERENCES

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