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## Reporting of serious toxicities of targeted cancer drugs in published reports of randomized phase III clinical trials (RCTs).

Health Services Research

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[Abstract]

**Background:** Information about safety of approved cancer drugs is updated regularly in drug labels on the basis of data from various sources. Here we compare serious toxicities of targeted cancer drugs obtained from the most recent drug labels to reporting of toxicities in articles describing RCTs that have evaluated these drugs. **Methods:** We searched for approved targeted cancer drugs with updated labels in years 2008/2009 in the U.S. Food and Drug Administration (FDA) website (FDA@Drugs). For each drug serious toxicities were identified in the "Warnings/Precautions" section of the label. Warnings related to pregnancy and prescribing were excluded. Published reports of RCTs referenced in the updated label of each drug were identified and searched for description of the corresponding serious toxicities. **Results:** We identified 12 eligible targeted drugs and 36 corresponding published reports of referenced RCTs. In total, 76 serious toxicities were reported in updated labels: 25% (N=19) were Black Box warnings and 49% (N=37) were explicitly mentioned as potentially fatal. Of these potentially fatal toxicities 59% (N=22) were not mentioned in labels at first approval of the drugs. Also, 38% (N=29) of all serious and 38% (N=14) of potentially fatal toxicities from updated labels were not reported explicitly in any published report of an RCT (Table). For serious toxicities from updated labels reported in RCTs (N=47) cumulative frequency of explicitly reported grade 3-4 potentially fatal toxicities was lower than for serious toxicities unlikely to prove fatal (1.8% [0.1%-8.4%] vs. 4.7% [0-47.7%], p=0.07). **Conclusions:** Toxicities that are not included in reports or are reported to be rarely severe in RCTs might be important cause of toxic death when these agents are used in general oncologic practice.

Drug (No. RCTs)	No. serious/No. potentially fatal toxicities from label	
	All	Not reported in any RCT
Bevacizumab (6)	9/5	2/1
Bortezomib (2)	9/1	4/0
Cetuximab (3)	5/3	2/2
Dasatinib (2)	4/1	1/0
Erlotinib (4)	10/7	4/1
Ibritumomab tiuxetan (2)	4/3	2/2
Imatinib (4)	8/1	3/1
Lapatinib (1)	4/1	2/1
Panitimumab (2)	4/1	1/1
Rituximab (5)	9/9	5/5
Sunitinib (2)	6/2	2/0
Trastuzumab (3)	4/3	1/0
	76/37	29/14

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