Prolonged Valsartan Use and Cancer Risk

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Background

- Generic valsartan was recalled in Hong Kong and amongst different localities because of suspicion on nitrosamines contamination.

FDA NEWS RELEASE

FDA announces voluntary recall of several medicines containing valsartan following detection of an impurity

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For Immediate Release: July 13, 2018

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Class 2 Medicines Recall: Teva UK Limited and Mylan - recall of some Valsartan containing products

Some valsartan containing products including certain batches supplied by Teva UK Limited and all unexpired batches supplied by Mylan are being recalled.

Published 30 November 2018
From: Medicines and Healthcare products Regulatory Agency

Recall of five valsartan-containing pharmaceutical products (with photos)
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The Department of Health (DH) today (July 6) instructed two licensed medicine wholesalers, namely Actavis Hong Kong Limited and Hong Kong Medical Supplies Ltd (HK Medical), to recall five products containing valsartan from the market as a precautionary measure due to an impurity detected in the raw material.

w of the possible health effects in pati
:hylamine (NDMA) – an impurity found in the active substance manufactured by
euticals.

https://www.gov.uk/drug-device-alerts/class-2-medicines-recall-teva-uk-limited-and-mylan-recall-of-some-valsartan-containing-products
https://www.info.gov.hk/gia/general/201807/06/P2018070600841.htm
https://www.ema.europa.eu/en/news/update-review-recalled-valsartan-medicines-preliminary-assessment-possible-risk-patients
https://www.fda.gov/news-events/press-announcements/fda-announces-voluntary-recall-several-medicines-containing-valsartan-following-detection-impurity

Objective

- To investigate the risk of cancer of patients with prolonged use of valsartan

Methods

- Treatment Group: Patients having prescriptions of Valsartan
- Control Group: Patients having prescriptions of Amlodipine
- Study Cohort:
  - Patients who had prescriptions of valsartan or amlodipine from 1st January 2003 to 30th June 2010
  - Patients were followed until a cancer outcome, death, loss to follow-up or end of study period (30th June 2019)
- Exclusion criteria:
  - Previously diagnosed with cancer
  - Prescribed with both medications
  - Taking medication for less than one year before cancer diagnosis
  - With follow-up period less than one year

Methods

- Primary outcome
  - Incidence of all cancer outcomes
  - Cancer diagnoses identified using International Classification of Diseases, 9th Revision (ICD-9)
- Supplementary analysis
  - Incidence of common types of cancer

Methods

- Data sources: the Clinical Data Analysis and Reporting System (CDARS) of the Hong Kong Hospital Authority
- Statistical analysis:
  - Crude cancer incidence rates were calculated as number of cancer occurrences per 10,000 person-years
  - Poisson regression was used to compare the cancer risk between valsartan cohort and amlodipine cohort

Results

Baseline Characteristics	Valsartan (N=5023)	Amlodipine (N=3692)
Sex (%):		
Male	2031 (40.4)	1667 (45.2)
Female	2992 (59.6)	2025 (54.8)
Age:		
Median (Interquartile range)	77.6 (67.1-86.5)	80.2 (68.6-88.5)
Duration of follow-up (%):		
Median (years)	10.97	12.12
<5	378 (7.5)	337 (9.1)
5-10	1035 (20.6)	260 (7.0)
>10	3610 (71.9)	3095 (83.8)
Charlson Comorbidity Index (%):		
0	581 (11.6)	702 (19.0)
1-2	2259 (45.0)	1672 (45.3)
3-4	1505 (30.0)	881 (23.9)
>=5	678 (13.5)	437 (11.8)

Results

Cohort	Valsartan (N=5023)	Amlodipine (N=3692)
Cancer Outcomes	887	740
Age and sex-adjusted incidences of cancer (per 10000 person-years)	168.67 (95% CI 157.92-180.01)	175.8 (95% CI 163.85-188.94)
Incidence rate ratio of valsartan relative to amlodipine	0.938 (95% CI 0.879-1.000)	

95% CI: 95% confidence interval

Results

Specific types of cancer	Incidence rate ratios of valsartan relative to amlodipine (per 10000 person-years)
Breast cancer	0.99 (95% CI 0.66-1.48)
Colorectal cancer	1.00 (95% CI 0.82-1.22)
Lung cancer	0.92 (95% CI 0.73-1.66)
Prostate cancer	0.92 (95% CI 0.58-1.46)

95% CI: 95% confidence interval

Conclusion

- Valsartan use was not associated with increased cancer incidence when compared to amlodipine during a follow-up period of more than 10 years.
- Clinicians could prescribe valsartan without concern for increased cancer risk, when risk of contamination is mitigated in the future.
- Patients should not stop taking valsartan abruptly without medical consultation.

Strengths and Limitations

- Strengths
  - Long duration of follow-up period
  - Use of regionwide registries
- Limitations
  - Lack of data regarding whether earlier batches of valsartan contained potentially carcinogenic contaminants

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