Recalled blood pressure drugs not linked to increased short term cancer risk

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Products containing the withdrawn blood pressure drug valsartan are not associated with a markedly increased short term risk of cancer, finds an expedited analysis published by *The BMJ* today.

The findings provide reassuring interim evidence about the risk of cancer in patients treated with valsartan products, but the authors say further studies are required to evaluate the risks for single cancers as well as longer term effects.

In July 2018, some valsartan products manufactured by the Chinese company Zhejiang Huahai Pharmaceuticals were suspected of having been contaminated with N-nitrosodimethylamine (NDMA), an impurity that can cause cancer.

Following the discovery, both European medical agencies and the US Food and Drug Administration (FDA) withdrew affected valsartan products from the market.

To better understand the possible consequences and help inform regulatory bodies about this potential public health issue, the Danish Medicines Agency collaborated with the University of Southern Denmark to assess the association between use of potentially NDMA contaminated valsartan products and risk of cancer.

Using data from Danish health registries, they included 5,150 patients aged 40 years and over with no previous cancer who used products containing valsartan between 1 January 2012 and 30 June 2018.

Based on product analysis and dose used, patients were classified as being exposed or not exposed to NDMA and were followed from one year after entering the study, for a median of 4.6 years, during which time cases of cancer were recorded.

After taking account of age, sex, and other potentially influential factors, the researchers found that, overall, exposure to potentially NDMA contaminated valsartan products showed no association with cancer compared with exposure to valsartan products that were not contaminated with NDMA. There was also no evidence of a dose-response pattern.

However, when they analysed single cancers, they found a slightly increased (but not statistically significant) risk of colorectal cancer and uterine cancer in patients exposed to NDMA. While they cannot fully explain this, it might require further study.

More importantly, the limited follow-up means that assessment of long-term effects is not possible, and the low number of events makes interpretation of estimates for single cancer outcomes difficult.

Nevertheless, the researchers believe that their results can support regulators in their evaluation of the potential public health impact of NDMA exposure via valsartan drugs—and provide some reassurance for people who might have been exposed.

They conclude: "Our results do not imply a marked increased short term overall cancer risk in users of valsartan contaminated with NDMA. However, uncertainty persists regarding single cancer outcomes, and studies with longer follow-up are needed to assess long-term cancer risk."

In a linked editorial, Rita Banzi and Vittorio Bertele' at the Center for Drug Regulatory Policies in Milan, Italy, say "this study alone cannot dispel doubts about the potential risk for patients in the longer term, but it helps inform decision-making around this episode."

"It also illustrates the usefulness of national registries for examining the relations between risk factors and health problems and how research can give a prompt response whenever public health concerns emerge," they add.

Regulatory actions coupled with the generation of robust evidence, they say "are the keys to responding promptly to emerging public health concerns."

More information: Use of N-nitrosodimethylamine (NDMA) contaminated valsartan products and risk of cancer: Danish nationwide cohort study, www.bmj.com/content/362/bmj.k3851

Editorial: Regulatory response to contaminated valsartan, www.bmj.com/content/362/bmj.k3855

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