# Safety of tumor necrosis factor inhibitor use in patients with concomitant malignancy


Hiep S. Phan B.S., Rick Weideman Pharm.D, Linda A. Feagins M.D.

VA North Texas Health Care System, Dallas, Texas and the University of Texas Southwestern Medical Center, Dallas, Texas


VA | U.S. Department of Veterans Affairs
Veterans Health Administration
*VA North Texas Health Care System*

UTSouthwestern Medical Center

## INTRODUCTION

**Tumor necrosis factor (TNF) inhibitors are considered contraindicated in patients with a history of malignancy. However, data to support this notion is limited with many sources inferring neutral or beneficial outcomes. We hypothesize TNF inhibitors can be used safely in patients with chronic inflammatory diseases, like inflammatory bowel disease (IBD), who have concomitant malignancy or develop malignancy while on these agents.**

## METHODS

- Retrospective chart review between 1996-2015 of patients seen at the VA North Texas Healthcare System
- Cases and controls (matched 1:2 for cancer type) were identified using pharmacy and pathology databases and then charts manually reviewed
- Cases were patients with inflammatory disease including inflammatory bowel disease (IBD), rheumatoid arthritis (RA), psoriatic arthritis (PsA), psoriasis or spondyloarthropathy (SpA), concomitant malignancy, and TNF inhibitor use
- Controls were patients with inflammatory disease, concomitant malignancy but no TNF inhibitor use.
- Data was collected for cases and controls including survival at 1-year, 2-years, 5-years after malignancy diagnosis and end of study time points.

## RESULTS

Table 1. Demographic data of veterans with inflammatory disease comparing patients exposed or not exposed to anti-TNF agents

| | Anti-TNF Exposed | Anti-TNF Naïve |
|---|---|---|
| Total No. of Patients | 36 | 70 |
| Sex | | |
| Male | 35 (97%) | 67 (96%) |
| Female | 1 (3%) | 3 (4%) |
| Ethnicity | | |
| Caucasian | 34 (94%) | 53 (76%) |
| African American | 1 (3%) | 13 (19%) |
| Hispanic | 1 (3%) | 3 (4%) |
| Native American | 0 (0%) | 1 (1%) |
| Inflammatory Disease Type | | |
| Inflammatory Bowel Disease only | | |
| Crohn's Disease | 1 (3%) | 3 (4%) |
| Ulcerative colitis | 2 (6%) | 3 (4%) |
| Rheumatoid Arthritis only | 22 (61%) | 44 (63%) |
| Psoriasis only | 3 (8%) | 12 (17%) |
| Spondylarthropathy only | | |
| Ankylosing Spondylitis | 2 (6%) | 2 (3%) |
| IBD + Spondylarthropathy | 1 (3%) | 0 (0%) |
| Psoriasis + Psoriatic Arthritis | 5 (14%) | 6 (9%) |
| Age of Inflammatory disease diagnosis (mean ± SD) | 46.7 ± 12.3 | 50.2 ± 15.2 |
| Inflammatory disease duration (years) (mean ± SD) | 21.7 ± 10.4 | 21.5 ± 15.2 |
| Charlson Comorbidity Index (mean ± SD) | 2.5 ± 1.7 | 2.0 ± 1.7 |
| Smoking Status | | |
| Never | 7 (19%) | 6 (9%) |
| Former | 18 (50%) | 30 (43%) |
| Active | 11 (31%) | 34 (49%) |

Table 2. Malignancy types, stage at diagnosis, and treatments for patients exposed or not exposed to anti-TNF agents. Cases matched 1:2 with controls for malignancy type.

| | Anti-TNF exposed | Anti-TNF naïve | p-value |
|---|---|---|---|
| Number of patients | 36 | 70 | |
| Age of malignancy diagnosis (mean + SD) | 62.8 ± 8.8 | 65.9 ± 8.1 | 0.25 |
| Cancer types | | | |
| Breast | 1 (3%) | 2 (3%) | -- |
| Colon | 1 (3%) | 2 (3%) | -- |
| Head & neck | 6 (17%) | 12 (17%) | -- |
| Hematologic | 3 (8%) | 3 (4%) | -- |
| Lung | 5 (14%) | 10 (14%) | -- |
| Prostate | 10 (28%) | 20 (29%) | -- |
| Renal | 4 (11%) | 8 (11%) | -- |
| Skin | 5 (14%) | 11 (16%) | -- |
| Urinary bladder | 1 (3%) | 2 (3%) | -- |
| Stage of Cancer diagnosis | | | |
| In Situ | 5 (14%) | 10 (14%) | 1.0 |
| Stage 1 | 16 (44%) | 20 (29%) | 0.13 |
| Stage 2 | 7 (19%) | 22 (31%) | 0.25 |
| Stage 3 | 2 (6%) | 10 (14%) | 0.21 |
| Stage 4 | 6 (17%) | 8 (11%) | 0.55 |
| Cancer treatments | | | |
| Chemotherapy | 4 (11%) | 13 (19%) | 0.41 |
| Hormonal | 2 (6%) | 3 (4%) | 1.0 |
| Radiation | 8 (22%) | 17 (24%) | 1.0 |
| Surgery | 25 (69%) | 51 (73%) | 0.82 |
| If TNF stopped, TNF restarted? | | | |
| 1 year | 4 (11%) | 0 | -- |
| 2 years | 8 (22%) | 0 | -- |
| 5 years | 2 (6%) | 0 | -- |
| End of study | 1 (3%) | 0 | -- |

Figure 1. Survival after cancer diagnosis for cases (anti-TNF exposed) and controls (anti-TNF naïve).

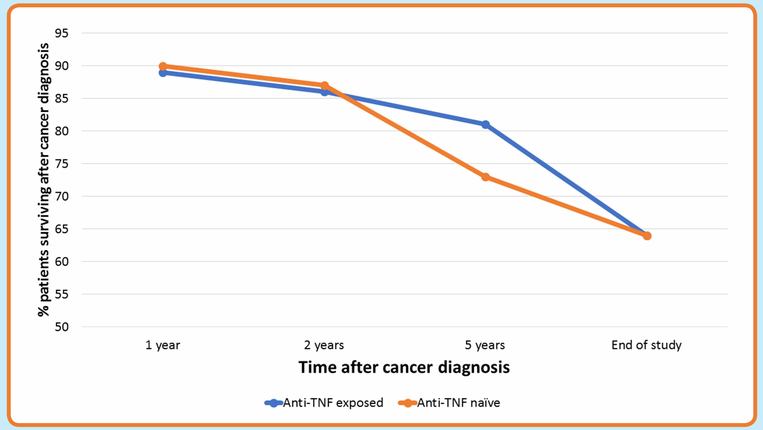
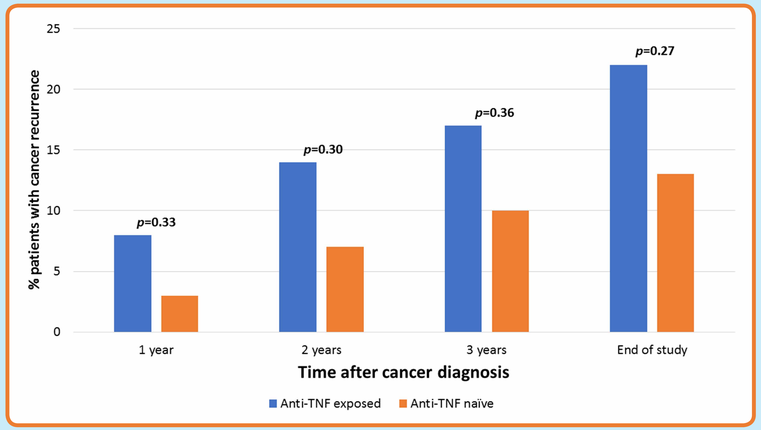



Figure 2. Cancer recurrence rates after initial cancer diagnosis for cases (anti-TNF exposed) and controls (anti-TNF naïve).




## CONCLUSIONS

- In matched cohorts of cancer patients with inflammatory diseases treated with or without TNF inhibitors, we found our patients had similar stages of disease at cancer diagnosis and underwent similar treatments for their cancers.
- Survival rates after a malignancy is diagnosed in patients with inflammatory diseases treated with TNF inhibitors are not statistically different from similar patients not treated with TNF inhibitors.
- Cancer recurrence rates after a malignancy is diagnosed in patients with inflammatory diseases treated with TNF inhibitors are not statistically different from similar patients not treated with TNF inhibitors.

## SPECULATIONS

**This preliminary data suggests that TNF inhibitors should not be withheld for fear of worsening survival or tumor recurrence after diagnosis with a malignancy if the agent is needed for adequate inflammatory disease control.**


This study was supported by the resources and use of facilities at the Department of Veteran's Affairs, Dallas, TX. The contents do not represent the views of the U.S. Department of Veteran Affairs or the United States Government.