



HAL
open science

Herpes Zoster and Vaccination Strategies in Inflammatory Bowel Diseases: A Practical Guide

Lucas Guillo, Christian Rabaud, Ernest Choy, Ferdinando D'amico, Silvio Danese, Siew Ng, Laurent Peyrin-Biroulet

► **To cite this version:**

Lucas Guillo, Christian Rabaud, Ernest Choy, Ferdinando D'amico, Silvio Danese, et al.. Herpes Zoster and Vaccination Strategies in Inflammatory Bowel Diseases: A Practical Guide. *Clinical Gastroenterology and Hepatology*, 2022, 20 (3), pp.481-490. 10.1016/j.cgh.2020.10.027 . hal-04167973

HAL Id: hal-04167973

<https://hal.univ-lorraine.fr/hal-04167973>

Submitted on 22 Jul 2024

HAL is a multi-disciplinary open access archive for the deposit and dissemination of scientific research documents, whether they are published or not. The documents may come from teaching and research institutions in France or abroad, or from public or private research centers.

L'archive ouverte pluridisciplinaire **HAL**, est destinée au dépôt et à la diffusion de documents scientifiques de niveau recherche, publiés ou non, émanant des établissements d'enseignement et de recherche français ou étrangers, des laboratoires publics ou privés.



Distributed under a Creative Commons Attribution - NonCommercial 4.0 International License

Herpes zoster and vaccination strategies in inflammatory bowel diseases: a practical guide

Lucas Guillo^{1,2}, Christian Rabaud³, Ernest H Choy⁴, Ferdinando D'Amico^{2,5}, Silvio Danese^{5,6}, Siew C Ng⁷, Laurent Peyrin-Biroulet²

1. Department of Gastroenterology, University Hospital of Marseille Nord, University of Aix-Marseille, Marseille, France.
2. Department of Gastroenterology and Inserm NGERE U1256, University Hospital of Nancy, University of Lorraine, Vandoeuvre-lès-Nancy, France.
3. Department of Infectious Disease, University Hospital of Nancy, University of Lorraine, Vandoeuvre-lès-Nancy, France.
4. CREATE Centre, Division of Infection and Immunity, Cardiff University, Cardiff, UK.
5. Department of Biomedical Sciences, Humanitas University, Pieve Emanuele, Milan, Italy.
6. IBD center, Department of Gastroenterology, Humanitas Clinical and Research Center - IRCCS, Rozzano, Milan, Italy.
7. Institute of Digestive Disease, Department of Medicine and Therapeutics, LKS Institute of Health Science, The Chinese University of Hong Kong, Hong Kong.

Corresponding author:

Prof. Laurent Peyrin-Biroulet, MD, PhD

Inserm NGERE U1256 and Department of Gastroenterology

Nancy University Hospital, University of Lorraine

1 Allée du Morvan, 54511 Vandoeuvre-lès-Nancy, France

Tel: (+33) 383153661 Fax: (+33) 383153633

E-mail: peyrinbiroulet@gmail.com

Word count: 5947 (main text and references)

Tables and figures: 5 tables

References: 98

Authors' Contributions

LG wrote the article. CR, EHC, FD, SD, SCN, and LPB critically revised the manuscript.

LPB supervised the study. The manuscript was approved by all authors.

Conflict of interest

L Guillo declares no conflict of interest. C Rabaud has served as a speaker, consultant and advisory board member for Astellas, Janssen, Gilead, Merck Sharp and Dohme. EH Choy has received research grants, honoraria and served as member of advisory boards and speaker bureaus of Abbvie, BioCancer, Biocon, Biogen, Bristol Myer Squibbs, Chugai Pharma, Eli Lilly, Gilead, Janssen, Merck Serono, Novartis, Pfizer, Regeneron, Roche, Sanofi and UCB. F D'Amico declares no conflict of interest. S Danese has served as a speaker, consultant, and advisory board member for Schering-Plough, AbbVie, Actelion, Alphawasserman, AstraZeneca, Cellerix, Cosmo Pharmaceuticals, Ferring, Genentech, Grunenthal, Johnson and Johnson, Millenium Takeda, MSD, Nikkiso Europe GmbH, Novo Nordisk, Nycomed, Pfizer, Pharmacosmos, UCB Pharma and Vifor. Siew C Ng has received research funds from Ferring and Abbvie, and speaker honorarium from Ferring, Abbvie, Takeda, Pfizer, Olympus, Tillotts, Menarini, Janssen. L Peyrin-Biroulet has served as a speaker, consultant and advisory board member for Merck, Abbvie, Janssen, Genentech, Mitsubishi, Ferring, Norgine, Tillots, Vifor, Hospira/Pfizer, Celltrion, Takeda, Biogaran, Boehringer-Ingelheim, Lilly, HAC- Pharma, Index Pharmaceuticals, Amgen, Sandoz, Forward Pharma GmbH, Celgene, Biogen, Lycera, Samsung Bioepis, Theravance.

Fundings

None.

Abstract (141 words)

Herpes zoster is a painful dermatomal cutaneous eruption due to the reactivation of the latent varicella-zoster virus. Patients with inflammatory bowel diseases have an increased risk of shingles compared to the general population and this risk can be increased with the use of immunosuppressive therapy. Live zoster vaccine and recombinant zoster vaccine have demonstrated efficacy for the prevention of herpes zoster. The recombinant zoster vaccine seems to offer greater efficacy and long-term protection profile compared with the live zoster vaccine. However, their use in clinical practice is still unclear and updated vaccination recommendations are lacking. This review will discuss risk for shingles in patients with inflammatory bowel diseases, available vaccines, and their efficacy and safety profiles. We will also provide guidance on who, when, and how to vaccinate for herpes zoster in routine clinical practice amongst patients with inflammatory bowel diseases.

Keywords: Herpes zoster, shingles, herpes zoster vaccine, inflammatory bowel diseases, Zostavax®, Shingrix®

Introduction

Herpes zoster (HZ), also known as shingles, is a painful dermatomal cutaneous eruption which occurs due to the reactivation of latent varicella-zoster virus (VZV)^{1,2}. Risk of HZ increases with old age and immunodeficiency conditions and its incidence rate (IR) is approximately 1.5 to 2-fold higher in immune-mediated inflammatory diseases (IMIDs) than in the general population³⁻⁵. Inflammatory bowel diseases (IBD) are also known to carry a higher risk of HZ^{5,6}. Corticosteroids, anti-tumor necrosis factor (anti-TNF) agents, and other biologics may increase the risk of opportunistic infections, including shingles^{7,8}. A recent meta-analysis showed that patients with immune mediated inflammatory disorders (IMIDs) have an overall increased risk of herpes zoster after treatment with Janus kinase (JAK) inhibitors⁹.

Live zoster vaccine (LZV) and non-live recombinant zoster vaccine (RZV) have both demonstrated efficacy for the prevention of HZ^{10,11}. Both are recommended in immunocompetent adults aged ≥ 60 years for LZV and aged ≥ 50 years for RZV^{12,13}. In 2015, the American College of Rheumatology (ACR) recommended vaccination with LZV for patients with rheumatoid arthritis (RA) aged ≥ 50 years before initiating biologics therapy¹⁴. In 2017, the American College of Gastroenterology (ACG) also recommended vaccination with LZV for patients with IBD aged ≥ 50 years¹⁵. Here, we reviewed available evidence regarding HZ risk in patients with IBD, discussed the efficacy and safety of HZ vaccination, and provided guidance for routine practice.

Risk for herpes zoster in IBD patients

Epidemiology and risk factors

In the general population, the IR of HZ ranges from 1.2 to 4.9 cases per 1,000 person-years (py)¹⁶⁻¹⁸. The incidence in IMIDs is approximately 1.5 to 2-fold higher than in the general population^{3,4,18-20}. In IBD, IR ranges from 6.67 to 9.2 cases per 1,000 py^{17,21,22}. Marehbian et al.²⁰ also reported a higher IR of 89 cases per 10,000 py with a ratio of 1.83 compared to the general population. Patients with Crohn's disease (CD) are at higher risk of shingles than those with ulcerative colitis (UC). IR ranges from 814 to 854 versus 664 to 670 cases per 100,000 py respectively for CD and UC^{19,23}. These results were confirmed in another study (IR 1.6 versus 1.2)⁶, and a meta-analysis of observational cohort studies, including more than 1,000,000 patients, reported a relative risk (RR) of 1.74 in CD and of 1.40 in UC compared to non-IBD patients²⁴. Finally, IBD activity is also a key factor for HZ, disease flare showed a hazard ratio (HR) of 3.69 (*Table 1*)¹⁷.

One established risk factors of shingles is the increased age^{1,3,25}. A meta-analysis of zoster infection risk found a RR of 1.65 with older age⁵. Regarding IBD, this age relationship is also observed in the occurrence of HZ. Gradual increase in risk is reported among over 60 years old (11.5 cases per 1000 py²¹, around 1,500 cases per 100,000 py¹⁹) and over 65 years old (15.48 cases per 1,000 py¹⁸, around 1200 cases per 100,000 py⁶). A significant increase in IR of HZ has also been noted in subjects over 45s (around 799 cases per 100,000 py⁶), and over 50s (11.02 cases per 1,000 py¹⁸, around 8 cases per 1,000 py²¹, around 1,100 cases per 100,000 py¹⁹). Furthermore, IR among those under 50s is approximately the same as the age group of the 50-60s in the general population¹⁹. A retrospective cohort study showed that in patients with IBD and IMIDs, the IRs among the 30s to 50s was similar or higher, respectively, than the corresponding rates in adults without IMIDs aged ≥ 60 ⁴. In a cohort including 108,604 IBD patients, patients with HZ had significantly more comorbidities including diabetes, cardiac conditions, liver or renal diseases, and chronic pulmonary diseases¹⁹. A meta-analysis confirmed that comorbidities such as diabetes, cardiovascular,

pulmonary, and renal diseases increased the risk of HZ (RR of 1.24 to 1.41)⁵. Moreover, female gender had a lower risk of HZ (RR=1.19)⁵. Likewise, ethnicity was identified as a risk factor for shingles. Asian patients had higher rates than north America, Europe, or Latin American populations; the incidence was particularly high in Japanese and Korean populations ranging from 10.4 to 18.34 cases per 1,000 py (*Table 1*)^{26,27}. Interestingly, a retrospective study demonstrated that IBD was ranked at the fourth position of the immunocompromising or chronic disease conditions with the highest rate of HZ, after the hematopoietic hematological transplant, hematological malignancy, and systemic lupus, in Japanese population²⁸. An ethnic genetic susceptibility is probably responsible to explain these differences of risk.

Treatment-related risk

Two retrospective observational cohort studies showed that 5-aminosalicylic acid (ASA) use was not associated with an increased risk of HZ^{6,19}, while a significant increase in shingles IR was found after therapy with corticosteroids (odds ratio (OR) of 1.5⁶ and 1.73¹⁹) and thiopurines (OR of 3.1⁶ and 1.85¹⁹). Another retrospective studies also reported an elevated risk of HZ with corticosteroids (HR of 1.27) and thiopurines (HR of 1.47) (*Table 2*)¹⁷.

Risk of shingles is also increased after treatment with anti-TNF agents. The OR ranges from 1.33 to 1.81 compared to patients with IBD not treated with anti-TNF drugs or who received 5-ASA^{19,20}. However, in a retrospective cohort of the United States Veterans Affairs Healthcare System (VAHS), which include 54,919 patients, anti-TNF agents alone were not associated with higher risk of zoster¹⁷. Combination therapy (anti-TNF agents and thiopurines) further increases the HZ risk with OR ranging from 1.65 to 3.68 (*Table 2*)^{17,19,20}. Colombel et al.²⁹ reviewed six major clinical trials on adalimumab comprising 3160 CD

patients. Of note, 46 cases of HZ were registered and 6 were considered severe²⁹. In the VARSITY trial, which compared adalimumab to vedolizumab in patients with UC, IR was 4.2 per 100 py in the adalimumab group³⁰. Although anti-TNF agents were associated with a higher risk of shingles in UC patients, there was no signal of developing severe forms of shingles with secondary bacterial infection or the requirement of an intravenous antiviral drug³¹.

Data concerning vedolizumab are reassuring. A retrospective study including data from six trials on vedolizumab reported an IR of 0.5 cases per 100 py³², and these findings were consistent with data from the VARSITY study (*Table 2*)³⁰. In the GEMINI I phase III trial, only two cases of HZ were detected in the vedolizumab arm and two cases were reported in the placebo arm³³. In the VAHS cohort, no HZ case was reported in IBD patients treated with vedolizumab¹⁷.

Safety data for ustekinumab are more limited. However, three major studies, CERTIFI, UNITI, and UNIFI, showed no increased risk of HZ³⁴⁻³⁶. Similarly, in a rheumatology study on psoriasis, no increased risk of shingles was found²³, but additional safety studies are necessary to confirm these findings (*Table 2*).

Tofacitinib, a pan-JAK inhibitor, has been approved for the treatment of patients with refractory UC³⁷. Tofacitinib was associated with an increased risk of HZ in both patients with RA and IBD, with an IR ranging from 3.4 to 4.1 cases per 100 py, and a dose dependent relationship (higher risk after 10 mg twice daily than 5 mg twice daily dosage) (*Table 2*)³⁸⁻⁴¹. A retrospective study, which including 1,157 UC patients treated with tofacitinib from 3 studies (induction, maintenance and long-term), showed IR of 3.45 and of 4.25 per 100 py at dosage of 5 mg and 10mg twice daily, respectively³⁸. Filgotinib and upadacitinib are selective JAK1-inhibitors currently being tested in both CD and UC and that should be available soon in routine practice. Approximately 1.3% and 1.4-2% of patients with RA developed HZ at a

daily dosage of 100 mg and 200 mg of filgotinib, respectively^{42,43}. Importantly, no significant difference was found in the rate of adverse events (AEs) between placebo and filgotinib groups⁴³. In a phase 2 study, HZ was detected in 3% of CD patients treated with daily dosage of 100 mg or 200 mg of filgotinib⁴⁴. Recently, a phase 2b/3 trial, which explored the use of filgotinib 100 mg or 200 mg once daily in patients with UC, reported low rates of HZ (from 0.4% to 0.8%) for both induction and maintenance phases, supporting the safety profile of the drug⁴⁵. Three phase 3 studies investigating the use of upadacitinib in patients with RA revealed that 0.5-1% and 1-2% of subjects receiving upadacitinib 15 mg or 30 mg once daily, developed HZ respectively⁴⁶⁻⁴⁸. In a phase 2 trial, one case of HZ was reported in CD patients receiving 12 mg (1.7%) and 24 mg (2.8%) once daily dose during the induction phase, and one case in the 24 mg (2.8%) once daily maintenance group⁴⁹. In a phase 2 trial, only one case of shingles (1.8%) was identified in UC patients treated with upadacitinib 45 mg once daily during the maintenance therapy⁵⁰. Further investigations are required to define whether selective JAK1-inhibitors (filgotinib and upadacitinib) are associated with a lower risk of developing HZ than tofacitinib. Immune response to HZ use JAK-signal transducer and activator of transcription (STAT) pathways, especially type I and II⁵¹. This explain why JAK-inhibitors have a strong link with shingles compared to other opportunistic infections. May be that selective JAK1-inhibitors disrupt the VZV response less than pan-JAK inhibitors.

Available vaccines

Live zoster vaccine (LZV): Zostavax[®]

Zostavax[®], an attenuated form of VZV, has been approved for the prevention of HZ and its complications in adults aged ≥ 60 years by the US Food and Drug Administration (FDA) since 2006¹², and adults aged ≥ 50 years by the European Medicines Agency⁵² (EMA) and the FDA⁵³ since 2008 and 2011, respectively. Instead, the US Advisory Committee on

Immunization Practices (ACIP) recommended the use of LZV since 2008 in adults aged ≥ 60 years¹². Zostavax[®] cost ranges from \$134.16 (Centers for Disease Control and Prevention (CDC) price) to \$216.66 (private price) per dose⁵⁴, but cost and reimbursement policy depend on individual country's healthcare system. A single dose administered subcutaneously or intramuscularly in the deltoid region is recommended and generally well tolerated¹⁰. Importantly, concomitant administration with a quadrivalent seasonal inactivated influenza vaccine (IIV4) and the 23-valent pneumococcal polysaccharide vaccine (PPSV23) is possible without loss of efficacy^{55,56}. Contraindications to LZV include primary and acquired immunodeficiency states (acute and chronic leukemias; lymphoma; other conditions affecting the bone marrow or lymphatic system; HIV/AIDS; cellular immune deficiencies), immunosuppressive therapy including high-dose corticosteroids, active untreated tuberculosis, and pregnancy (*Table 3*)⁵².

Recombinant zoster vaccine (RZV): Shingrix[®]

Shingrix[®] is approved for the prevention of HZ and its complications among adults aged ≥ 50 years by the US FDA since 2017¹³, and the EMA since 2018⁵⁷. The US ACIP recommended it since 2018 for adults aged ≥ 50 years¹³. Shingrix[®] cost ranges from \$101.51 (CDC price) to \$151.51 (private price) per dose⁵⁸, but its price and reimbursement depend on the country and healthcare system. To date, it is available only in the US, Canada, and China. Two doses administered intramuscularly in the deltoid region 2-6 months apart are recommended^{11,59}. Concomitant administration with IIV4 and PPSV23 is possible without loss of efficacy^{60,61}. RZV is also effective in case of previous vaccination with LZV in adults over 65 years old⁶². Main contraindications are the hypersensitivity to the active substance or to any excipient. Administration of RZV to immunocompromised subjects should be based on careful consideration of potential benefits and risks (*Table 3*)⁵⁷.

Efficacy and safety data

Efficacy data

It has been demonstrated that a single dose of LZV was immunogenic in adults aged over 60s⁶³. In addition, response was significantly lower in patients aged over 70s⁶³. The Zostavax Efficacy and Safety Trial (ZEST) reported an efficacy of 69.8% to prevent HZ in adults aged 50-59 years⁶⁴, while the Shingles Prevention Study (SPS) reported an efficacy of 51.3% in adults aged over 60 years and 37.6% in subjects over 70 years⁶⁵. Efficacy rates based on different age groups are as follows: 69.8% in the 50-59s, 63.9% in the 60-69s and 37.6% in the over 70s^{64,65}. Two studies found that LZV was protective for about five years^{66,67}. However, short-term and long-term studies showed that vaccine efficacy tended to decrease in the second year, with rates of 62.0%, 48.9%, and 44.6% at year 1, 2, and 4 respectively⁶⁷. Moreover, this rate decreased to 21.1% after 11 years (*Table 4*)⁶⁸. A retrospective study recruiting 463,541 patients with IMIDs (RA, psoriasis, psoriatic arthritis, ankylosing spondylitis, and IBD) showed that patients vaccinated with LZV had a lower IR of HZ than unvaccinated patients during a median follow-up of 2 years⁶⁹. In the VAHS cohort, including 39,983 patients, vaccination in IBD patients was associated with a significant reduction of HZ risk versus unvaccinated patients (adjusted hazard ratio of 0.54)⁷⁰. Finally, Winthrop et al.⁷¹ reported that LZV did not provide adequate long-term protection in a study assessing RA patients treated with tofacitinib.

Concerning RZV, immunogenicity studies showed a dose-dependent relationship, and a two-dose schedule produced 1.5 to 2.5-fold greater humoral immunity than a single dose^{72,73}. The ZOE-50 and ZOE-70 studies reported an efficacy against HZ of 97.2% in the over 50 years and of 89.8% in the over 70 years, respectively^{74,75}. Furthermore, vaccine efficacy did not differ between different age groups. Efficacy rates across different age groups

were as follows: 96.6 to 96.9% in the 50-59s, 94.1 to 97.4% in the 60-69s, and 89.8 to 97.9% in the over 70s⁷⁴. RZV was also associated with reduced pain symptoms and risk of postherpetic neuralgia in case of breakthrough shingles^{76,77}. Shingrix[®] is protective for at least four years and a minimal decline in efficacy is described during this period, with rates of 97.6% and 87.9% at one and four years, respectively (*Table 4*)⁷⁵. Further data showed that responses remained substantially above the pre-vaccination level for up to nine years, and a statistical model predicted that the immune responses remained above the pre-vaccination level for up to 15 years⁷⁸. In a retrospective study including 403 patients with RA and other systemic rheumatic diseases who received RZV, only three cases of HZ occurred 11 months after vaccination⁷⁹. Recently, Kochhar et al. demonstrated that HZ risk was significantly lower in IBD patients receiving 2 doses of RZV compared to those who did not (OR 0.62) , but they were still at higher risk than the general population who received 2 doses(OR 3.03)⁸⁰. However, the reliability of these preliminary results in RA and IBD remains to be confirmed with additional data. Long-term efficacy data in immunocompromised subjects and booster schedule are missing.

Safety profile

The most frequent local and systemic AEs after LZV vaccination are injection-site reaction of mild to moderate intensity (48.3%) and headache (9.4%) (*Table 3*)^{64,65,81}. Zostavax[®] can be safely used in patients treated with methotrexate, thiopurines, or low to intermediate dose of corticosteroids (<20 mg/day of prednisone or equivalent)⁸². Safety data about anti-TNF agents are reassuring. A retrospective study reported no case of HZ within 42 days of vaccination in 59 IBD patients who were treated with an anti-TNF agent⁸³. Zhang et al.⁶⁹ also found no case of HZ within 42 days of vaccination in a large cohort of 551 patients with IMIDs (117 IBD) receiving anti-TNF drugs. On the other hand, an observational cohort

study showed an increased risk of HZ (45 per 1,000 py) in the 42 days after vaccination in patients taking immunosuppressant drugs (e.g. azathioprine, methotrexate, etanercept...) and antirejection drugs (e.g. tacrolimus, cyclosporine...) ⁸⁴. However, in this cohort 83.9% of patients were taking high and low dose corticosteroids either alone or combined with other immunosuppressant agents, justifying the higher risk of shingles. Interestingly, Winthrop et al. ⁸⁵ found that patients who began tofacitinib 2-3 weeks after receiving LZV had similar immune response to those in the placebo group at week 14.

RZV demonstrated a good safety profile. Injection-site reaction of mild to moderate intensity was the most frequent AE varying from 74.1% to 81.5% of patients ^{74,75}. Myalgia, fatigue, and headache were the most common systemic reactions ranging from 1.4% to 2.4% of patients (*Table 3*) ^{74,75}. Similarly, a recent prospective study assessing IBD patients showed a 74.6% rate of local AEs and a low rate of flares (1.5%) after vaccination with RZV ⁸⁶. Of note, a systematic review reported that RZV had a RR of 1.79 for injection-site events when compared with LZV ⁸⁷. Four phase 3 studies highlighted that RZV was immunogenic and humoral responses persisted for at least 12 months after vaccination in immunocompromised adults with solid tumors on chemotherapy, post renal transplantation, hematologic malignancies, and autologous hematopoietic stem cell transplant ⁸⁸⁻⁹¹. Although the use of RZV in immunodeficiency situations seems reassuring, data on IBD patients are lacking. In addition, impact of vaccine on IBD course is unknown.

Who, when, and how to vaccinate patients with IBD?

Among patients with IBD who were followed in the nationwide VAHS cohort, only 20.96% of patients were vaccinated against shingles ⁹², and the median age at the time of vaccination was 64.9 years ⁸³. In another study, the rate of HZ vaccination was of 15.5 per 1,000 py ²². These data revealed the low vaccination coverage and the delay in access to

vaccination. In IMiDs patients aged 30 to 50 years, IR of HZ was similar or higher than the corresponding IR in healthy adults aged ≥ 60 years⁴, suggesting that vaccination should be considered earlier in this population. Ethnicity may affect the risk of HZ. Asian population has a higher risk for HZ than Caucasian populations (10.4 to 18.34 cases per 1,000py)^{26,27}, and this risk is more pronounced with tofacitinib treatment^{38,39,93}. The SELECT-SUNRISE study, which tested upadacitinib at 30 mg once daily dosage in RA, also reported a higher risk of HZ in Japanese population compared with the non-Japanese population (6% vs 1-2%)⁹⁴. In 2015, the ACR recommended vaccination with LZV for patients with RA aged ≥ 50 years before initiating biologics therapy or Tofacitinib¹⁴. In 2017, the ACG clinical guidelines for IBD recommended that patients over 50 years, including those immunosuppressed, should be considered for HZ vaccination¹⁵. These guidelines encourage increased access to vaccination for IBD patients. HZ is the most frequent vaccine-preventable disease in patients with IBD compared to others (e.g. pneumococcal, influenza or hepatitis)⁹⁵. Vaccination with RZV appears to be better than LZV both in terms of efficacy and duration of protection^{87,96}. Moreover, a recent cost-efficacy study comparing both vaccines demonstrated that RZV had a lower cost-efficacy ratio than LZV⁹⁷. For this reason, in 2018 the US ACIP recommended RZV use rather than LZV in immunocompetent adults aged ≥ 50 years¹³.

Updated vaccination recommendations for the prevention of HZ are still lacking for patients with IBD. To guide physicians for HZ vaccination in IBD, we propose that RZV should be considered in patients aged ≥ 50 years with or without immunosuppressive therapies (including high dose corticosteroids (≥ 20 mg/day of prednisone or equivalent), biologics, or JAK inhibitors), in adult patients before starting treatment with biologics or JAK-inhibitors (tofacitinib, upadacitinib or filgotinib) regardless of age, and in populations at high risk (Asian population, family history of zoster, comorbidities (diabetes, cardiovascular, pulmonary and renal chronic disease)) regardless of age. If RZV is not available, LZV should

be considered in patients aged ≥ 50 years without immunosuppressive therapies, in adult patients before starting treatment with biologics or tofacitinib regardless of age, and in populations at high risk. LZV use in patients treated with immunosuppressive therapies should be avoided. In addition, vaccination with RZV should be considered after LZV to prevent loss of protection (*Table 5*). LZV should be administered at least 3 weeks prior to commencement of immunomodulator therapy and subsequent immunization can only be administered after a 3–6 month cessation of immunosuppressive therapy⁸. Concerning VZV negative patients (history or serology), a retrospective study showed that incidence of HZ in vaccinated children with VZV is 5 times lower compared to children who contract wildtype VZV⁹⁸. Hence, these patients should be vaccinated with VZV vaccine in order to prevent VZV infection as recommended⁸, but also for HZ.

Table 1: Risk factors for herpes zoster infection

Factor	Risk
Older age	RR 1.65 (based on a meta-analysis)
Female	RR 1.19 (based on a meta-analysis)
Comorbidities*	RR 1.24 – 1.41(based on a meta-analysis)
Crohn’s disease	RR 1.74 (based on a meta-analysis)
Ulcerative colitis	RR 1.40 (based on a meta-analysis)
Inflammatory bowel disease	6.67 to 9.2 cases per 1,000py (based on 3 population-based studies)
Disease flare-up	HR 3.69 (based on a population-based study)
Asian population	10.4 to 18.34 cases per 1,000py (based on 2 population-based studies)

HR, hazard ratio; py; person-years; RR, relative risk;

* Comorbidities: diabetes, cardiovascular, pulmonary and renal chronic disease;

Table 2: Risk related to available treatment

Treatment	Risk
5-Aminosalicylic acid	No risk (based on 2 retrospective cohort studies)
Corticosteroids	OR 1.5 – 1.73 (based on 2 retrospective cohort studies) HR 1.27 (based on a population-based study)
Thiopurines	OR 1.85 – 3.1 (based on 2 retrospective cohort studies) HZ 1.47 (based on a population-based study)

Anti-tumor necrosis factor	OR 1.33 – 1.81 (based on 2 retrospective studies)
Combination therapy	OR 1.65- 3.68 (based on 2 retrospective studies and 1 population-based study)
Vedolizumab	IR 0.5 cases per 100py (based on 1 RCT and 1 post hoc analysis from 6 trials)
Ustekinumab	Reassuring data (based on 3 randomized controlled trial and 1 review article)
Tofacitinib	IR 3.4 – 4.1 cases per 100py (based on 4 post hoc safety analysis studies)

HR, hazard ratio, IR, incidence rate; OR, odds ratio;

Table 3: Comparison of vaccines’ characteristics

Category	Live zoster vaccine	Recombinant zoster vaccine
FDA approval	2006	2017
ACIP recommendation	≥ 60 years	≥ 50 years
Cost	\$134.16 (CDC price) to \$216.66 (private price) per dose	\$101.51 (CDC price) to \$151.51 (private price) per dose
Number of doses	Single 0.65 ml dose	Two 0.5 ml doses
Spacing between dose	Not available	2-6 months
Storage	Freezer: -50°C to -15°C (-58°F to 5°F)	Refrigerator: 2°C to 8°C (36°F to 46°F)
Administration	Subcutaneous injection in deltoid	Intramuscular injection in deltoid
Concomitant validated administration	IIV4 and PPSV23	IIV4 and PPSV23
Contraindications	Primary and acquired immunodeficiency states (acute and chronic leukemias; lymphoma; other conditions affecting the bone marrow or lymphatic system; HIV/AIDS; cellular immune deficiencies), immunosuppressive therapy including high-dose corticosteroids, active untreated tuberculosis, and pregnancy	Hypersensitivity to the active substance or any excipient
Injection site reactions	48.3%	74.1 to 81.5%
Adverse events	Headache	Myalgia, fatigue, and headache

ACIP, Advisory Committee on Immunization Practices; CDC, Centers for Disease Control and Prevention; FDA, Food and Drug Administration; IIV4, quadrivalent seasonal inactivated influenza vaccine; PPSV23, 23-valent pneumococcal polysaccharide vaccine; HIV/AIDS, human immunodeficiency virus/acquired immuno-deficiency syndrome;

Table 4: Comparison of vaccines' efficacy

Category	Live zoster vaccine	Recombinant zoster vaccine
50 to 59 years	69.8%	96.6 - 96.9%
60 to 69 years	63.9%	94.1 - 97.4%
≥ 60 years	37.6%	89.8 - 97.9%
Year 1	62%	97.6%
Year 4	44.6%	87.9%

Table 5: Proposed recommendations

Vaccines	Aged ≥ 50 years without immunosuppressive therapies*	Aged ≥ 50 years under immunosuppressive therapies*	Before starting biologics or JAK inhibitors	Population at high-risk**
Recombinant zoster vaccine	Yes	Yes	Yes	Yes
Live zoster vaccine	Yes, if RZV is not available***	Should be avoided	Yes, if RZV is not available***	Yes, if RZV is not available***

* Including high dose corticosteroids (≥20 mg/day of prednisone or equivalent), biologics, or JAK inhibitor;

** Asian population, comorbidities (diabetes, cardiovascular, pulmonary and renal chronic disease);
*** Vaccination with RZV should be considered LZV to prevent loss effective protection;

References

1. Cohen JI. Clinical practice: Herpes zoster. *N Engl J Med* 2013;369:255-63.
2. Mahalingam R, Wellish M, Wolf W, et al. Latent varicella-zoster viral DNA in human trigeminal and thoracic ganglia. *N Engl J Med* 1990;323:627-31.
3. Kawai K, Yawn BP. Risk Factors for Herpes Zoster: A Systematic Review and Meta-analysis. *Mayo Clin Proc* 2017;92:1806-21.
4. Yun H, Yang S, Chen L, et al. Risk of Herpes Zoster in Autoimmune and Inflamm
Yun H, Yang S, Chen L, et al. Risk of Herpes Zoster in Autoimmune and Inflammatory Diseases: Implications for Vaccination. *Arthritis Rheumatol* 2016;68:2328-37.
5. Marra F, Parhar K, Huang B, et al. Risk Factors for Herpes Zoster Infection: A Meta-Analysis. *Open Forum Infect Dis* 2020;7:ofaa005.
6. Gupta G, Lautenbach E, Lewis JD. Incidence and risk factors for herpes zoster among patients with inflammatory bowel disease. *Clin Gastroenterol Hepatol* 2006;4:1483-90.
7. Toruner M, Loftus EV, Harmsen WS, et al. Risk factors for opportunistic infections in patients with inflammatory bowel disease. *Gastroenterology* 2008;134:929-36.
8. Rahier JF, Magro F, Abreu C, et al. Second European evidence-based consensus on the prevention, diagnosis and management of opportunistic infections in inflammatory bowel disease. *J Crohns Colitis* 2014;8:443-68.
9. Olivera PA, Lasa JS, Bonovas S, et al. Safety of Janus Kinase Inhibitors in Patients With Inflammatory Bowel Diseases or Other Immune-mediated Diseases: A Systematic Review and Meta-Analysis. *Gastroenterology* 2020;158:1554-73.e12.
10. Keating GM. Shingles (Herpes Zoster) Vaccine (Zostavax®): A Review in the Prevention of Herpes Zoster and Postherpetic Neuralgia. *BioDrugs* 2016;30:243-54.
11. Syed YY. Recombinant Zoster Vaccine (Shingrix®): A Review in Herpes Zoster. *Drugs Aging* 2018;35:1031-40.
12. Harpaz R, Ortega-Sanchez IR, Seward JF, et al. Prevention of herpes zoster: recommendations of the Advisory Committee on Immunization Practices (ACIP). *MMWR Recomm Rep* 2008;57:1-30.
13. Dooling KL, Guo A, Patel M, et al. Recommendations of the Advisory Committee on Immunization Practices for Use of Herpes Zoster Vaccines. *MMWR Morb Mortal Wkly Rep* 2018;67:103-8.
14. Singh JA, Saag KG, Bridges SL, et al. 2015 American College of Rheumatology Guideline for the Treatment of Rheumatoid Arthritis. *Arthritis Care Res* 2016;68:1-25.
15. Farraye FA, Melmed GY, Lichtenstein GR, et al. ACG Clinical Guideline: Preventive Care in Inflammatory Bowel Disease. *Am J Gastroenterol*. 2017;112:241-58.
16. Yawn BP, Saddier P, Wollan PC, et al. A population-based study of the incidence and

- complication rates of herpes zoster before zoster vaccine introduction. *Mayo Clin Proc* 2007;82:1341-9.
17. Khan N, Patel D, Trivedi C, et al. Overall and Comparative Risk of Herpes Zoster With Pharmacotherapy for Inflammatory Bowel Diseases: A Nationwide Cohort Study. *Clin Gastroenterol Hepatol* 2018;16:1919-27.e3.
 18. Chen S-Y, Suaya JA, Li Q, et al. Incidence of herpes zoster in patients with altered immune function. *Infection*. 2014;42:325-34.
 19. Long MD, Martin C, Sandler RS, et al. Increased risk of herpes zoster among 108 604 patients with inflammatory bowel disease. *Aliment Pharmacol Ther* 2013;37:420-9.
 20. Marehbian J, Arrighi HM, Hass S, et al. Adverse events associated with common therapy regimens for moderate-to-severe Crohn's disease. *Am J Gastroenterol* 2009;104:2524-33.
 21. Côté-Daigneault J, Bessissow T, Nicolae MV, et al. Herpes Zoster Incidence in Inflammatory Bowel Disease Patients: A Population-Based Study. *Inflamm Bowel Dis* 2019;25:914-8.
 22. Nugent Z, Singh H, Targownik LE, Bernstein CN. Herpes Zoster Infection and Herpes Zoster Vaccination in a Population-Based Sample of Persons With IBD: Is There Still an Unmet Need? *Inflamm Bowel Dis* 2019;25:532-40.
 23. Côté-Daigneault J, Peerani F, MacMahon E, et al. Management and Prevention of Herpes Zoster in the Immunocompromised Inflammatory Bowel Disease Patient: A Clinical Quandary. *Inflamm Bowel Dis* 2016;22:2538-47.
 24. Ning L, Liu R, Li S, et al. Increased risk of herpes zoster infection in patients with inflammatory bowel disease: a meta-analysis of cohort studies. *Eur J Clin Microbiol Infect Dis* 2020;39:219-27.
 25. Kawai K, Gebremeskel BG, Acosta CJ. Systematic review of incidence and complications of herpes zoster: towards a global perspective. *BMJ Open* 2014;4:e004833.
 26. Kim YJ, Lee CN, Lim C-Y, et al. Population-based study of the epidemiology of herpes zoster in Korea. *J Korean Med Sci* 2014;29:1706-10.
 27. Chang K, Lee H-S, Kim Y-J, et al. Increased Risk of Herpes Zoster Infection in Patients With Inflammatory Bowel Diseases in Korea. *Clin Gastroenterol Hepatol* 2018;16:1928-36.e2.
 28. Imafuku S, Dormal G, Goto Y, et al. Risk of herpes zoster in the Japanese population with immunocompromising and chronic disease conditions: Results from a claims database cohort study, from 2005 to 2014. *J Dermatol* 2020;47:236-44.
 29. Colombel J-F, Sandborn WJ, Panaccione R, et al. Adalimumab safety in global clinical trials of patients with Crohn's disease. *Inflamm Bowel Dis* 2009;15:1308-19.
 30. Sands BE, Peyrin-Biroulet L, Loftus EV, et al. Vedolizumab versus Adalimumab for Moderate-to-Severe Ulcerative Colitis. *N Engl J Med* 2019;381:1215-26.
 31. Khan N, Trivedi C, Shah Y, et al. The Severity of Herpes Zoster in Inflammatory Bowel Disease Patients Treated With Anti-TNF Agents. *Inflamm Bowel Dis* 2018;24:1274-79.
 32. Colombel J-F, Sands BE, Rutgeerts P, et al. The safety of vedolizumab for ulcerative colitis and Crohn's disease. *Gut* 2017;66:839-51.
 33. Feagan BG, Rutgeerts P, Sands BE, et al. Vedolizumab as Induction and Maintenance Therapy for Ulcerative Colitis. *N Engl J Med* 2013;369:699-710.
 34. Feagan BG, Sandborn WJ, Gasink C, et al. Ustekinumab as Induction and Maintenance Therapy for Crohn's Disease. *N Engl J Med* 2016;375:1946-60.
 35. Sands BE, Sandborn WJ, Panaccione R, et al. Ustekinumab as Induction and Maintenance Therapy for Ulcerative Colitis. *N Engl J Med* 2019;381:1201-14.
 36. Sandborn WJ, Gasink C, Gao L-L, et al. Ustekinumab Induction and Maintenance

- Therapy in Refractory Crohn's Disease. *N Engl J Med* 2012;367:1519-28.
37. Sandborn WJ, Su C, Sands BE, et al. Tofacitinib as Induction and Maintenance Therapy for Ulcerative Colitis. *N Engl J Med* 2017;376(18):1723-36.
 38. Winthrop KL, Melmed GY, Vermeire S, et al. Herpes Zoster Infection in Patients With Ulcerative Colitis Receiving Tofacitinib. *Inflamm Bowel Dis* 2018;24:2258-65.
 39. Winthrop KL, Curtis JR, Lindsey S, et al. Herpes Zoster and Tofacitinib: Clinical Outcomes and the Risk of Concomitant Therapy. *Arthritis Rheumatol* 2017;69:1960-8.
 40. Sandborn WJ, Panés J, D'Haens GR, et al. Safety of Tofacitinib for Treatment of Ulcerative Colitis, Based on 4.4 Years of Data From Global Clinical Trials. *Clin Gastroenterol Hepatol* 2019;17:1541-50.
 41. Wollenhaupt J, Lee E-B, Curtis JR, et al. Safety and efficacy of tofacitinib for up to 9.5 years in the treatment of rheumatoid arthritis: final results of a global, open-label, long-term extension study. *Arthritis Res Ther* 2019;21:89.
 42. Genovese MC, Kalunian K, Gottenberg J-E, et al. Effect of Filgotinib vs Placebo on Clinical Response in Patients With Moderate to Severe Rheumatoid Arthritis Refractory to Disease-Modifying Antirheumatic Drug Therapy: The FINCH 2 Randomized Clinical Trial. *JAMA* 2019;322:315-25.
 43. Westhovens R, Taylor PC, Alten R, et al. Filgotinib (GLPG0634/GS-6034), an oral JAK1 selective inhibitor, is effective in combination with methotrexate (MTX) in patients with active rheumatoid arthritis and insufficient response to MTX: results from a randomised, dose-finding study (DARWIN 1). *Ann Rheum Dis* 2017;76:998-1008.
 44. Vermeire S, Schreiber S, Petryka R, et al. Clinical remission in patients with moderate-to-severe Crohn's disease treated with filgotinib (the FITZROY study): results from a phase 2, double-blind, randomised, placebo-controlled trial. *Lancet* 2017;389:266-75.
 45. Gilead and Galapagos Announce Positive Topline Results of Phase 2b/3 Trial of Filgotinib in Moderately to Severely Active Ulcerative Colitis. <https://www.gilead.com/news-and-press/press-room/press-releases/2020/5/gilead-and-galapagos-announce-positive-topline-results-of-phase-2b3-trial-of-filgotinib-in-moderately-to-severely-active-ulcerative-colitis>. Accessed on 18 June 2020.
 46. Burmester GR, Kremer JM, Van den Bosch F, et al. Safety and efficacy of upadacitinib in patients with rheumatoid arthritis and inadequate response to conventional synthetic disease-modifying anti-rheumatic drugs (SELECT-NEXT): a randomised, double-blind, placebo-controlled phase 3 trial. *Lancet* 2018;391:2503-12.
 47. Genovese MC, Fleischmann R, Combe B, et al. Safety and efficacy of upadacitinib in patients with active rheumatoid arthritis refractory to biologic disease-modifying anti-rheumatic drugs (SELECT-BEYOND): a double-blind, randomised controlled phase 3 trial. *Lancet* 2018;391:2513-24.
 48. Fleischmann R, Pangan AL, Song I-H, et al. Upadacitinib Versus Placebo or Adalimumab in Patients With Rheumatoid Arthritis and an Inadequate Response to Methotrexate: Results of a Phase III, Double-Blind, Randomized Controlled Trial. *Arthritis Rheumatol* 2019;71:1788-800.
 49. Sandborn WJ, Feagan BG, Loftus EV, et al. Efficacy and Safety of Upadacitinib in a Randomized Trial of Patients With Crohn's Disease. *Gastroenterology* 2020;158:2123-38.e8.
 50. Sandborn WJ, Ghosh S, Panes J, et al. Efficacy of Upadacitinib in a Randomized Trial of Patients With Active Ulcerative Colitis. *Gastroenterology* 2020;158:2139-49.e14.
 51. Ghoreschi K, Laurence A, O'Shea JJ. Janus kinases in immune cell signaling. *Immunol Rev* 2009;228:273-87.
 52. European Medicines Agency. Zostavax, herpes zoster vaccine live: EU summary of product characteristics. <https://www.ema.europa.eu/en/medicines/human/EPAR/zostavax>. Accessed on 18 June 2020.

53. Hales CM, Harpaz R, Ortega-Sanchez I, et al. Update on Recommendations for Use of Herpes Zoster Vaccine. *MMWR Morb Mortal Wkly Rep* 2014;63:729-31.
54. Center for Disease Control and Prevention. CDC Vaccine Price List 6-1-2018. <https://www.cdc.gov/vaccines/programs/vfc/awardees/vaccine-management/price-list/2018/2018-06-01.html>. Accessed on 18 June 2020.
55. Kerzner B, Murray AV, Cheng E, et al. Safety and Immunogenicity Profile of the Concomitant Administration of ZOSTAVAX and Inactivated Influenza Vaccine in Adults Aged 50 and Older. *J Am Geriatr Soc* 2007;55:1499-507.
56. MacIntyre CR, Egerton T, McCaughey M, et al. Concomitant administration of zoster and pneumococcal vaccines in adults ≥ 60 years old. *Hum Vaccin* 2010;6:894-902.
57. European Medicines Agency. Shingrix, herpes zoster vaccine (recombinant, adjuvanted): summary of product characteristics. <https://www.ema.europa.eu/en/medicines/human/EPAR/shingrix>. Accessed on 18 June 2020.
58. Center for Disease Control and Prevention. CDC Vaccine Price List 6-1-2020. <https://www.cdc.gov/vaccines/programs/vfc/awardees/vaccine-management/price-list/index.html>. Accessed on 18 June 2020.
59. GSK. Shingrix (zoster vaccine recombinant, adjuvanted): US prescribing information. 2017. https://gsksource.com/pharma/content/dam/GlaxoSmithKline/US/en/Prescribing_Information/Shingrix/pdf/SHINGRIX.PDF. Accessed on 18 June 2020.
60. Schwarz TF, Aggarwal N, Moeckesch B, et al. Immunogenicity and Safety of an Adjuvanted Herpes Zoster Subunit Vaccine Coadministered With Seasonal Influenza Vaccine in Adults Aged 50 Years or Older. *J Infect Dis* 2017;216:1352-61.
61. Maréchal C, Lal H, Poder A, et al. Immunogenicity and safety of the adjuvanted recombinant zoster vaccine co-administered with the 23-valent pneumococcal polysaccharide vaccine in adults ≥ 50 years of age: A randomized trial. *Vaccine* 2018;36:4278-86.
62. Grunning K, Campora L, Douha M, et al. Immunogenicity and Safety of the HZ/su Adjuvanted Herpes Zoster Subunit Vaccine in Adults Previously Vaccinated With a Live Attenuated Herpes Zoster Vaccine. *J Infect Dis* 2017;216:1343-51.
63. Levin MJ, Oxman MN, Zhang JH, et al. Varicella-Zoster Virus-Specific Immune Responses in Elderly Recipients of a Herpes Zoster Vaccine. *J Infect Dis* 2008;197:825-35.
64. Schmader KE, Levin MJ, Gnann JW, et al. Efficacy, Safety, and Tolerability of Herpes Zoster Vaccine in Persons Aged 50-59 Years. *Clin Infect Dis* 2012;54:922-8.
65. Oxman MN, Levin MJ, Johnson GR, et al. A Vaccine to Prevent Herpes Zoster and Postherpetic Neuralgia in Older Adults. *N Engl J Med* 2005;352:2271-84.
66. Yun H, Xie F, Baddley JW, Winthrop K, et al. Longterm Effectiveness of Herpes Zoster Vaccine among Patients with Autoimmune and Inflammatory Diseases. *J Rheumatol* 2017;44:1083-7.
67. Schmader KE, Oxman MN, Levin MJ, et al. Persistence of the Efficacy of Zoster Vaccine in the Shingles Prevention Study and the Short-Term Persistence Substudy. *Clin Infect Dis* 2012;55:1320-8.
68. Morrison VA, Johnson GR, Schmader KE, et al. Long-term persistence of zoster vaccine efficacy. *Clin Infect Dis* 2015;60:900-9.
69. Zhang J, Xie F, Delzell E, et al. Association Between Vaccination for Herpes Zoster and Risk of Herpes Zoster Infection Among Older Patients With Selected Immune-Mediated Diseases. *JAMA* 2012;308:43-9.
70. Khan N, Trivedi C, Kavani H, et al. Efficacy of Live Attenuated Herpes Zoster Vaccine in Patients With Inflammatory Bowel Diseases. *Clin Gastroenterol Hepatol* 2019;17(7):1341-7.
71. Winthrop KL, Wouters A, Choy EH, et al. Long-term effectiveness of live herpes

- zoster vaccine in patients with rheumatoid arthritis subsequently treated with tofacitinib. *Ann Rheum Dis* 2020;79:669-71.
72. Chlibek R, Smetana J, Pauksens K, et al. Safety and immunogenicity of three different formulations of an adjuvanted varicella-zoster virus subunit candidate vaccine in older adults: A phase II, randomized, controlled study. *Vaccine* 2014;32:1745-53.
 73. Chlibek R, Bayas JM, Collins H, et al. Safety and Immunogenicity of an AS01-adjuvanted Varicella-zoster Virus Subunit Candidate Vaccine Against Herpes Zoster in Adults ≥ 50 Years of Age. *J Infect Dis* 2013;208:1953-61.
 74. Lal H, Cunningham AL, Godeaux O, et al. Efficacy of an Adjuvanted Herpes Zoster Subunit Vaccine in Older Adults. *N Engl J Med* 2015;372:2087-96.
 75. Cunningham AL, Lal H, Kovac M, et al. Efficacy of the Herpes Zoster Subunit Vaccine in Adults 70 Years of Age or Older. *N Engl J Med* 2016;375:1019-32.
 76. Kovac M, Lal H, Cunningham AL, et al. Complications of herpes zoster in immunocompetent older adults: Incidence in vaccine and placebo groups in two large phase 3 trials. *Vaccine* 2018;36:1537-41.
 77. Curran D, Oostvogels L, Heineman T, et al. Quality of Life Impact of an Adjuvanted Recombinant Zoster Vaccine in Adults Aged 50 Years and Older. *J Gerontol A Biol Sci Med Sci* 2019;74:1231-8.
 78. Schwarz TF, Volpe S, Catteau G, et al. Persistence of immune response to an adjuvanted varicella-zoster virus subunit vaccine for up to year nine in older adults. *Hum Vaccines Immunother* 2018;14:1370-7.
 79. Stevens E, Weinblatt ME, Massarotti E, et al. Safety of the Zoster Vaccine Recombinant Adjuvanted in Rheumatoid Arthritis and Other Systemic Rheumatic Disease Patients: A Single Center's Experience With 400 Patients. *ACR Open Rheumatol* 2020;2:357-61.
 80. Kochhar G, Desai A, Sandhu DS, et al. Effectiveness of recombinant zoster vaccine (Shingrix) in patients with inflammatory bowel disease. *Gastroenterology* 2020;158:S-55.
 81. Simberkoff MS. Safety of Herpes Zoster Vaccine in the Shingles Prevention Study: A Randomized Trial. *Ann Intern Med* 2010;152:545-54.
 82. Meroni PL, Zavaglia D, Girmenia C. Vaccinations in adults with rheumatoid arthritis in an era of new disease-modifying anti-rheumatic drugs. *Clin Exp Rheumatol* 2018;36:317-28.
 83. Khan N, Shah Y, Trivedi C, et al. Safety of herpes zoster vaccination among inflammatory bowel disease patients being treated with anti-TNF medications. *Aliment Pharmacol Ther* 2017;46:668-72.
 84. Cheetham TC, Marcy SM, Tseng H-F, et al. Risk of Herpes Zoster and Disseminated Varicella Zoster in Patients Taking Immunosuppressant Drugs at the Time of Zoster Vaccination. *Mayo Clin Proc* 2015;90:865-73.
 85. Winthrop KL, Wouters AG, Choy EH, et al. The Safety and Immunogenicity of Live Zoster Vaccination in Patients With Rheumatoid Arthritis Before Starting Tofacitinib: A Randomized Phase II Trial. *Arthritis Rheumatol* 2017;69:1969-77.
 86. Satyam VR, Li P-H, Reich J, et al. Safety of Recombinant Zoster Vaccine in Patients with Inflammatory Bowel Disease. *Dig Dis Sci* 2020;S10620-019-06016-4.
 87. Tricco AC, Zarin W, Cardoso R, et al. Efficacy, effectiveness, and safety of herpes zoster vaccines in adults aged 50 and older: systematic review and network meta-analysis. *BMJ*. 2018;363:k4029.
 88. Vink P, Delgado Mingorance I, Maximiano Alonso C, et al. Immunogenicity and safety of the adjuvanted recombinant zoster vaccine in patients with solid tumors, vaccinated before or during chemotherapy: A randomized trial. *Cancer* 2019;125:1301-12.
 89. Vink P, Ramon Torrell JM, Sanchez Fructuoso A, et al. Immunogenicity and Safety of

the Adjuvanted Recombinant Zoster Vaccine in Chronically Immunosuppressed Adults Following Renal Transplant: a Phase 3, Randomized Clinical Trial. *Clin Infect Dis* 2020;70:181-90.

90. Dagnev AF, Ilhan O, Lee W-S, et al. Immunogenicity and safety of the adjuvanted recombinant zoster vaccine in adults with haematological malignancies: a phase 3, randomised, clinical trial and post-hoc efficacy analysis. *Lancet Infect Dis* 2019;19:988-1000.
91. Bastidas A, de la Serna J, El Idrissi M, et al. Effect of Recombinant Zoster Vaccine on Incidence of Herpes Zoster After Autologous Stem Cell Transplantation: A Randomized Clinical Trial. *JAMA* 2019;322:123-33.
92. Khan N, Trivedi C, Kavani H, et al. Frequency of Herpes Zoster Vaccination Among Inflammatory Bowel Disease Patients. *Inflamm Bowel Dis* 2019;25:345-51.
93. Winthrop KL, Yamanaka H, Valdez H, et al. Herpes zoster and tofacitinib therapy in patients with rheumatoid arthritis. *Arthritis Rheumatol* 2014;66:2675-84.
94. Kameda H, Takeuchi T, Yamaoka K, et al. Efficacy and safety of upadacitinib in Japanese patients with rheumatoid arthritis (SELECT-SUNRISE): a placebo-controlled phase IIb/III study. *Rheumatology* 2020;keaa084.
95. Vinsard DG, Wakefield D, Vaziri H, et al. Vaccine-Preventable Diseases in Hospitalized Patients With Inflammatory Bowel Disease: A Nationwide Cohort Analysis. *Inflamm Bowel Dis* 2019;25:1966-73.
96. Burnett H, McGirr A, Widenmaier R, et al. Vaccines for Herpes Zoster: A Systematic Review of Randomized Controlled Trials In Adults ≥ 50 Years of Age. *Value Health* 2017;20:A780.
97. Prosser LA, Harpaz R, Rose AM, et al. A Cost-Effectiveness Analysis of Vaccination for Prevention of Herpes Zoster and Related Complications: Input for National Recommendations. *Ann Intern Med* 2019;170:380-8.
98. Weinmann S, Chun C, Schmid DS, et al. Incidence and clinical characteristics of herpes zoster among children in the varicella vaccine era, 2005-2009. *J Infect Dis* 2013;208:1859-68.

What You Need to Know

Background: Patients with IBD have an increased risk of HZ compared to the general population and this risk can be increased with the use of immunosuppressive therapies.

Findings: LVZ and RZV are currently available for the prevention of HZ. RZV offer a greatest efficacy against HZ and better long-term protection than LZV. However, to date, RZV is not recommended in patients with IBD.

Implications for patient care: RZV should be considered as a first-line approach when it is available for HZ prevention.